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L14             1 S TOFIMILAST/CN
L15             1 S PUMAFENTRINE/CN

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L18             2 S L16 AND L17
L19          5523 S ANTICHOLINERGIC
L20            31 S L16 AND L19
L21             9 S L20 AND (PY<2003 OR AY<2003 OR PRY<2003)
L22          3212 S PDE4 OR PDEIV OR (PDE 4) OR (PDE IV) OR (PHOSPHODIESTERASE(W)
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L27            48 S L24 AND L26

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     FILE 'HCAPLUS' ENTERED AT 10:29:11 ON 06 FEB 2009
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L29             3 S L22 AND L28
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SESSION RESUMED IN FILE 'HCAPLUS' AT 13:46:46 ON 04 FEB 2009
FILE 'HCAPLUS' ENTERED AT 13:46:46 ON 04 FEB 2009
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   31.05     217.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                   -4.10      -4.10

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=> s knowles
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=> s phosphodiesterase
L9        28991 PHOSPHODIESTERASE

=> s l8 and l9
L10           0 L8 AND L9

=> s phosphodiesterase and anticholinergic
          28991 PHOSPHODIESTERASE
           5521 ANTICHOLINERGIC
L11          43 PHOSPHODIESTERASE AND ANTICHOLINERGIC

=> s l11 and PY=2003
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L12           6 L11 AND PY=2003

=> d l12 1-6 ti

L12  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Pharmaceutical compositions based on anticholinergics and additional
     active ingredients

L12  ANSWER 2 OF 6  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Prokinetic agents for treating gastric hypomotility and related disorders

L12  ANSWER 3 OF 6  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Bladder, bowel and sexual dysfunction in multiple sclerosis. Management
     strategies

L12  ANSWER 4 OF 6  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Phosphodiesterase 4 inhibitor in combination with
     anticholinergic agent for treating pulmonary diseases

L12  ANSWER 5 OF 6  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Therapy of chronic obstructive pulmonary disease

L12  ANSWER 6 OF 6  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Preparation of nitrosated and nitrosylated compounds and their use for
     treating respiratory disorders
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=> d l12 1-6 ti abs bib

L12  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Pharmaceutical compositions based on anticholinergics and additional
     active ingredients
AB   A pharmaceutical composition comprising an anticholinergic and at
     least one addnl. active ingredient selected from among corticosteroids,
     dopamine agonists, PDE-IV inhibitors, NK1-antagonists, endothelin
     antagonists, antihistamines, and EGFR-kinase inhibitors, processes for
     preparing them and their use in the treatment of respiratory diseases.  Among
     a number of compds. prepared was N-[2-[3,5-bis(trifluoromethyl)phenyl]ethyl]-2-
     [4-[(3-hydroxypropyl)methylamino]piperidin-1-yl]-N-methyl-2-
     phenylacetamide.  Inhalable powders include a formulation containing
     tiotropium bromide, budesonide, and lactose.
AN   2005:586215  HCAPLUS <<LOGINID::20090204>>
DN   143:120526
TI   Pharmaceutical compositions based on anticholinergics and additional
     active ingredients
IN   Pairet, Michel; Pieper, Michael P.; Meade, Christopher John Montague;
     Reichl, Richard; Schmelzer, Christel; Jung, Birgit
PA   Boehringer Ingelheim Pharma GmbH & Co. Kg, Germany
SO   U.S. Pat. Appl. Publ., 50 pp., Cont.-in-part of U.S. Ser. No. 824,391.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 19
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     DE 10062712         A1     20020620   DE 2000-10062712         20001215
     DE 10063957         A1     20020627   DE 2000-10063957         20001220
     DE 10110772         A1     20020912   DE 2001-10110772         20010307
     DE 10111058         A1     20020912   DE 2001-10111058         20010308
     DE 10113366         A1     20020926   DE 2001-10113366         20010320
     DE 10138272         A1     20030227   DE 2001-10138272         20010810 <--
     US 20020151541      A1     20021017   US 2001-7182             20011019
     US 20020183292      A1     20021205   US 2001-86145            20011019
     CA 2614631          A1     20020510   CA 2001-2614631          20011023
     US 20020137764      A1     20020926   US 2001-40196            20011025
     US 20020122773      A1     20020905   US 2001-27662            20011220
     DE 10206505         A1     20030828   DE 2002-10206505         20020216 <--
     US 20020169181      A1     20021114   US 2002-92116            20020306 <--
     US 6620438          B2     20030916
     US 20020193393      A1     20021219   US 2002-93240            20020307
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     US 6608054          B2     20030819
     US 20030158196      A1     20030821   US 2003-360064           20030207 <--
     US 20030181478      A1     20030925   US 2003-395777           20030324 <--
     US 6890517          B2     20050510
     US 20030203925      A1     20031030   US 2003-413065           20030414 <--
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     US 6696042          B2     20040224
     US 20040024007      A1     20040205   US 2003-613783           20030703
     US 20040151770      A1     20040805   US 2004-763894           20040123
     US 20040161386      A1     20040819   US 2004-775901           20040210
     US 20040176338      A1     20040909   US 2004-776757           20040211
     US 20040192675      A1     20040930   US 2004-824391           20040414
     US 20050147564      A1     20050707   US 2005-68134            20050228
     AU 2008202554       A1     20080703   AU 2008-202554           20080610
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PRAI	DE 2000-10054042	A	20001031
	US 2000-253613P	P	20001128
	DE 2000-10062712	A	20001215
	DE 2000-10063957	A	20001220
	US 2000-257220P	P	20001221
	US 2000-257221P	P	20001221
	DE 2001-10110772	A	20010307
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	DE 2001-10113366	A	20010320
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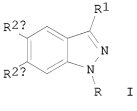
	US 2001-281857P	P	20010405
	US 2001-281874P	P	20010405
	DE 2001-10138272	A	20010810
	US 2001-314599P	P	20010824
	US 2001-7182	B1	20011019
	US 2001-86145	B1	20011019
	US 2001-27662	B1	20011220
	DE 2002-10206505	A	20020216
	US 2002-92116	A1	20020306
	US 2002-93240	B1	20020307
	US 2002-100659	A1	20020318
	US 2002-369213P	P	20020401
	US 2003-360064	A2	20030207
	US 2003-413065	B2	20030414
	US 2003-419358	A1	20030421
	US 2003-613783	A2	20030703
	US 2004-763894	A2	20040123
	US 2004-775901	A2	20040210
	US 2004-776757	A2	20040211
	US 2004-824391	A2	20040414
	CA 2001-2436540	A3	20011023
	US 2001-40196	B1	20011025
	US 2003-395777	A1	20030324
	AU 2006-202723	A3	20060626
OS	MARPAT 143:120526		

L12 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Prokinetic agents for treating gastric hypomotility and related disorders

GI



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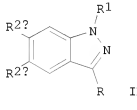

II

AB Stasis is treated or prevented in all or any part or parts of the stomach of a patient, especially a human patient, in need of such treatment, where said stasis results from hypomotility in the stomach, particularly gastric hypomotility with delayed emptying of the liquid and/or solid contents of the stomach. Gastric or gastrointestinal disorders are also treated which are characterized by one or more symptoms selected from pain, nausea, vomiting, heartburn, postprandial discomfort, indigestion and gastroesophageal reflux. Such treatment or prevention is achieved by administering to the patient a therapeutically effective amount of an

inhibitor of phosphodiesterase-4 (PDE4), including isoenzyme subtypes thereof, sufficient to treat or prevent such hypomotility or gastric or gastrointestinal disorder in said patient. The PDE4 inhibitor comprises I or II [preferrably R = cyclopentyl or cyclohexyl; R1 = (C1-C2) alkyl; one of R2a and R2b = H and the other = Q; dashed line = single bond; m = 0, R113 and R114 are cis to each other; R113 = CN, R115 = H, R114 = carboxy, -CH2OH, -CH2C(=O)NH2]. Pharmaceutical compns. are also described which are useful for carrying out the above-mentioned methods of treatment and prevention, and which are also useful in the treatment of a gastric or gastrointestinal disorder in a patient which comprises with respect to said patient, (i) a sign or concomitant of diabetic neuropathy, anorexia nervosa, achlorhydria, gastrointestinal surgery, post-surgical recovery in the period of emergence from general anesthesia; or the administration of morphine and morphine-like opioids; (ii) a secondary aspect of a primary disease or disorder in said patient which is organic, wherein said disease or disorder involves particularly a gastroenteric or gastroesophageal organ or tissue, or an organ or tissue of the central nervous system of said patient; or (iii) an adverse side effect of a different therapeutic agent administered to said patient in the course of treating another unrelated disease or disorder in said patient.

AN 2003:737369 HCAPLUS <<LOGINID::20090204>>
DN 139:255368
TI Prokinetic agents for treating gastric hypomotility and related disorders
IN Watson, John W.; Andrews, Paul L. R.; Woods, Anthony J.
PA USA
SO U.S. Pat. Appl. Publ., 57 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 20030176421	A1	20030918	US 1999-476253	19991230 <--
PRAI US 1999-476253		19991230		

OS MARPAT 139:255368

L12 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Bladder, bowel and sexual dysfunction in multiple sclerosis. Management strategies
AB A review. Although patients with multiple sclerosis (MS) are likely to have problems with bladder, bowel and sexual function, these problems have often been neglected in the past. Bladder dysfunction produces symptoms of urgency, frequency and urge incontinence (due to bladder overactivity and incomplete emptying), and is found in up to 75% of patients with MS. The mainstay of drug treatment for neurogenic bladder overactivity is anticholinergic therapy, although intravesical treatments have also been proposed, such as the vanilloids and botulinum toxin, as well as sublingual cannabinoids. There has been much progress with proerectile agents in recent years, notably the use of sildenafil citrate, which has been shown to be particularly effective in these patients. Other agents include apomorphine-HCl and newer phosphodiesterase 5 inhibitors; however, the efficacy of these drugs in patients with MS remains to be proven. Research in female sexual dysfunction is also progressing, although this aspect of patient well-being has only recently been addressed; the reported development of a classification system for the condition is likely to help categorize future treatments. Unlike bladder and sexual dysfunction, there have been rather limited advances in the treatment of fecal incontinence and constipation specifically for patients with MS, despite a prevalence of up to 50%. This review highlights the strategies for these types of dysfunction which are commonly seen in patients with MS, with report of recent pharmacol.

developments.
AN 2003:154025 HCAPLUS <<LOGINID::20090204>>
DN 138:280644
TI Bladder, bowel and sexual dysfunction in multiple sclerosis. Management strategies
AU Das Gupta, Ranan; Fowler, Clare J.
CS Department of Uro-Neurology, National Hospital for Neurology and Neurosurgery, London, UK
SO Drugs (2003), 63(2), 153-166
CODEN: DRUGAY; ISSN: 0012-6667
PB Adis International Ltd.
DT Journal; General Review
LA English
RE.CNT 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Phosphodiesterase 4 inhibitor in combination with anticholinergic agent for treating pulmonary diseases
AB This invention relates to treating pulmonary diseases such as obstructive pulmonary disease or asthma by administering a phosphodiesterase 4 (PDE4) inhibitor in combination with an anticholinergic agent. Assays showed that inhibition of the rolipram low affinity site of PDE4 is associated with the desired action. Inhalant, nasal and tablet formulations containing cilomilast as PDE4 inhibitor and tiotropium or tiotropium bromide as anticholinergic agent are given.
AN 2003:117610 HCAPLUS <<LOGINID::20090204>>
DN 138:131124
TI Phosphodiesterase 4 inhibitor in combination with anticholinergic agent for treating pulmonary diseases
IN Knowles, Richard Graham; Ward, Peter
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003011274	A2	20030213	WO 2002-EP8322	20020725 <--
	WO 2003011274	A3	20030918		
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	AU 2002321261	A1	20030217	AU 2002-321261	20020725 <--
	EP 1411914	A2	20040428	EP 2002-754939	20020725
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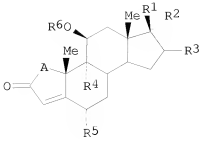
	HU 2004001614	A2	20041129	HU 2004-1614	20020725
	CN 1551763	A	20041201	CN 2002-817396	20020725
	JP 2004538302	T	20041224	JP 2003-516505	20020725
	US 20040180918	A1	20040916	US 2004-484292	20040120

	ZA 2004000410	A	20041013	ZA 2004-410	20040120
	IN 2004DN00154	A	20050401	IN 2004-DN154	20040121
	NO 2004000353	A	20040326	NO 2004-353	20040126
	MX 2004000793	A	20040521	MX 2004-793	20040126
PRAI	GB 2001-18373	A	20010727		
	WO 2002-EP8322	W	20020725		

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Therapy of chronic obstructive pulmonary disease
AB A review. Chronic obstructive pulmonary disease is one of the commonest causes of morbidity and mortality in the world, and is increasing in prevalence. Current therapies are not very effective, and no current treatment prevents the relentless progression of airflow limitation that characterizes this disease. Smoking cessation is the only strategy that reduces this decline in lung function, and although Bupropion is the most effective aid to quitting, more effective treatments of nicotine addiction are needed. The mainstay of treatment is bronchodilators for symptom relief, and inhaled anticholinergics and β2-agonists are useful by reducing hyperinflation of the lungs. A new once-daily inhaled anticholinergic is the most effective bronchodilator, but long-acting inhaled β2-agonists are also useful. Theophylline is used as an addnl. bronchodilator in more severe patients, and may have some anti-inflammatory action. In contrast, inhaled corticosteroids are poorly effective and do not reduce disease progression, although recent studies with combination inhalers (corticosteroid + long-acting β2-agonist) have shown better effects. Long-term oxygen therapy is needed by patients with pulmonary hypertension and right heart failure. There is a pressing need to develop new classes of therapy, and several new drugs are current in development, including interleukin-8 antagonists, phosphodiesterase-4 inhibitors, protease inhibitors, and antioxidants.
AN 2002:951293 HCAPLUS <<LOGINID::20090204>>
DN 139:16913
TI Therapy of chronic obstructive pulmonary disease
AU Barnes, Peter J.
CS National Heart and Lung Institute, Department of Thoracic Medicine, Imperial College, London, SW3 6LY, UK
SO Pharmacology & Therapeutics (2003), 97(1), 87-94
CODEN: PHTHDT; ISSN: 0163-7258
PB Elsevier Science Inc.
DT Journal; General Review
LA English
RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Preparation of nitrosated and nitrosylated compounds and their use for treating respiratory disorders
GI



I

AB Disclosed are (i) compds. of a steroid, a β-agonist, an anticholinergic, a mast cell stabilizer, and a phosphodiesterase (PDE) inhibitor directly or indirectly linked to a NO or NO2 group or a group which stimulates endogenous production of NO or EDRF in vivo; (ii) compns. of steroids, β-agonists, anticholinergics, mast cell stabilizers, and PDE inhibitors, which can optionally be substituted with at least one NO or NO2 moiety or a group which stimulates endogenous production of NO or EDRF in vivo, and a compound that donates, transfers or releases nitric oxide as a charged species, i.e., nitrosonium or nitroxyl, or as the neutral species, nitric oxide (NO) or that stimulates endogenous production of NO or EDRF in vivo; and (iii) uses for them in preventing and/or treating respiratory disorders. E.g., I [CH:CH, CH2CH2; R1 = COCH2BD (B = O, S; D = NO, NO2, CRdOC(O)Y(CReRf)pTQ (Rd = H, alkyl, aryl, etc.; Re, Rf = H, alkyl, alkylamino, carboxy, etc.; p = 1-6; T = covalent bond, O, S, N; Q = NO, NO2), etc.; R2, R3 = H, OH, alkyl, etc.; R4, R5 = H, halo; R6 = H, D) (defined as above), etc.] were prepared E.g., reaction of 3-mercapto-3-methylbutyric acid and 2,4,6-trimethoxybenzyl alc. gave 3-methyl-3-(2,4,6-trimethoxyphenylmethylthio)butyric acid. The last was reacted with 6α-fluoro-11β,21-dihydroxy-16α,17α-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione. Deprotection of the product, followed by reaction with tert-Bu nitrite, gave 6α-fluoro-11β-hydroxy-16α,17α-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione-21-[3-methyl-3-nitrosothio]butanoate. The measurement of biol. activity in a pulmonary model of allergic asthma and lung inflammation was undertaken in adult sheep.

AN 1997:640643 HCAPLUS <<LOGINID::20090204>>
DN 127:318553
OREF 127:62425a,62428a

TI Preparation of nitrosated and nitrosylated compounds and their use for treating respiratory disorders

IN Garvey, David S.; Letts, L. Gordon; Renfroe, H. Burt; Richardson, Stewart K.
PA Nitromed, Inc., USA; Garvey, David S.; Letts, L. Gordon; Renfroe, H. Burt; Richardson, Stewart K.

SO PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

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US 5824669	A	19981020	US 1996-620882	19960322

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     AU 9725336           A     19971010    AU 1997-25336          19970319
     AU 733202            B2    20010510
     EP 904266            A1    19990331    EP 1997-916818         19970319
          R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, FI
     JP 2000509016        T     20000718    JP 1997-533628         19970319
     US 6197762           B1    20010306    US 1998-157242         19980918
     US 37116             E1    20010327    US 1998-219476         19981223
     US 6579863           B1    20030617    US 2000-689851         20001013 <--
     US 20030199529       A1    20031023    US 2003-428936         20030505 <--
     US 7160920           B2    20070109
     US 20070155781       A1    20070705    US 2006-604677         20061128
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OS   MARPAT 127:318553


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L7             0 S KNOWLES/AP
L8           273 S KNOWLES
L9         28991 S PHOSPHODIESTERASE
L10            0 S L8 AND L9
L11           43 S PHOSPHODIESTERASE AND ANTICHOLINERGIC
L12            6 S L11 AND PY=2003

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CA SUBSCRIBER PRICE                                    -9.02      -9.02

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Connecting via Winsock to STN



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 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  NOV 21  CAS patent coverage to include exemplified prophetic
                  substances identified in English-, French-, German-,
                  and Japanese-language basic patents from 2004-present
 NEWS  3  NOV 26  MARPAT enhanced with FSORT command
 NEWS  4  NOV 26  CHEMSAFE now available on STN Easy
 NEWS  5  NOV 26  Two new SET commands increase convenience of STN
                  searching
 NEWS  6  DEC 01  ChemPort single article sales feature unavailable
 NEWS  7  DEC 12  GBFULL now offers single source for full-text
                  coverage of complete UK patent families
 NEWS  8  DEC 17  Fifty-one pharmaceutical ingredients added to PS
 NEWS  9  JAN 06  The retention policy for unread STNmail messages
                  will change in 2009 for STN-Columbus and STN-Tokyo
 NEWS 10  JAN 07  WPIDS, WPINDEX, and WPIX enhanced Japanese Patent
                  Classification Data
 NEWS 11  FEB 02  Simultaneous left and right truncation (SLART) added
                  for CERAB, COMPUAB, ELCOM, and SOLIDSTATEM
 NEWS 12  FEB 02  GENBANK enhanced with SET PLURALS and SET SPELLING

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
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* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 17:41:38 ON 05 FEB 2009

=> file registry
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.22       0.22

FILE 'REGISTRY' ENTERED AT 17:41:46 ON 05 FEB 2009
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provided by InfoChem.
```

STRUCTURE FILE UPDATES: 4 FEB 2009 HIGHEST RN 1100909-82-7
DICTIONARY FILE UPDATES: 4 FEB 2009 HIGHEST RN 1100909-82-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> exp N-(3,5-dichloro-1-oxidopyridin-4-yl)-8-methoxy-2-(trifluoromethyl)quinoline-5-carboxamide/cn

E1	1	N-(3,5-DICARBOXYPHENYL)MALEIMIDE/CN
E2	1	N-(3,5-DICARBOXYPHENYL)OCTADECYLAMIDE 1-HYDROXY-2-NAPHTHOIC ACID/CN
E3	0 -->	N-(3,5-DICHLORO-1-OXIDOPYRIDIN-4-YL)-8-METHOXY-2-(TRIFLUOROMETHYL)QUINOLINE-5-CARBOXAMIDE/CN
E4	1	N-(3,5-DICHLORO-1-OXOPYRIDIN-4-YL)-2-(5-(4-FLUOROBENZYL)PYRROLO(2,1-B)THIAZOL-7-YL)-2-(OXO)ACETAMIDE/CN
E5	1	N-(3,5-DICHLORO-1-OXOPYRIDIN-4-YL)-2-(7-(4-FLUOROBENZYL)PYRROLO(1,2-B)PYRIDAZIN-5-YL)-2-(OXO)ACETAMIDE/CN
E6	1	N-(3,5-DICHLORO-1-OXOPYRIDIN-4-YL)-3-(6-(1-(METHANESULFONYL)-1-METHYLETHYL)QUINOLIN-8-YL)BENZAMIDE/CN
E7	1	N-(3,5-DICHLORO-1-OXOPYRIDIN-4-YL)-4-DIFLUOROMETHOXY-3-CYCLOPROPYLMETHOXYBENZAMIDE/CN
E8	1	N-(3,5-DICHLORO-2,6-DIFLUOROPYRID-4-YL)-3-CYCLOPENTYLOXY-4-METHOXYBENZAMIDE/CN
E9	1	N-(3,5-DICHLORO-2-HYDROXY-4-METHYLPHENYL)-N'-(1,1,3,3-TETRAMETHYLBUTYL)UREA/CN
E10	1	N-(3,5-DICHLORO-2-HYDROXY-4-METHYLPHENYL)-N'-(2,6-DIMETHYLPHENYL)UREA/CN
E11	1	N-(3,5-DICHLORO-2-HYDROXY-4-METHYLPHENYL)-N'-(3,4,5-TRIMETHOXYPHENYL)UREA/CN
E12	1	N-(3,5-DICHLORO-2-HYDROXY-4-METHYLPHENYL)-N'-(3,5-DICHLOROPHENYL)UREA/CN

=> exp N-(3,5-dichloro-1-oxo-pyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide/cn

E1	1	N-(3,5-DICARBOXYPHENYL)MALEIMIDE/CN
E2	1	N-(3,5-DICARBOXYPHENYL)OCTADECYLAMIDE 1-HYDROXY-2-NAPHTHOIC ACID/CN
E3	0 -->	N-(3,5-DICHLORO-1-OXO-PYRIDIN-4-YL)-2-1-(4-FLUOROBENZYL)-5-HYDROXY-1H-INDOL-3-YL -2-OXOACETAMIDE/CN
E4	1	N-(3,5-DICHLORO-1-OXOPYRIDIN-4-YL)-2-(5-(4-FLUOROBENZYL)PYRROLO(2,1-B)THIAZOL-7-YL)-2-(OXO)ACETAMIDE/CN
E5	1	N-(3,5-DICHLORO-1-OXOPYRIDIN-4-YL)-2-(7-(4-FLUOROBENZYL)PYRROLO(1,2-B)PYRIDAZIN-5-YL)-2-(OXO)ACETAMIDE/CN
E6	1	N-(3,5-DICHLORO-1-OXOPYRIDIN-4-YL)-3-(6-(1-(METHANESULFONYL)-1-METHYLETHYL)QUINOLIN-8-YL)BENZAMIDE/CN
E7	1	N-(3,5-DICHLORO-1-OXOPYRIDIN-4-YL)-4-DIFLUOROMETHOXY-3-CYCLOPROPYLMETHOXYBENZAMIDE/CN

```
E8              1     N-(3,5-DICHLORO-2,6-DIFLUOROPYRID-4-YL)-3-CYCLOPENTYLOXY-4-M
                      ETHOXYBENZAMIDE/CN
E9              1     N-(3,5-DICHLORO-2-HYDROXY-4-METHYLPHENYL)-N'-(1,1,3,3-TETRAM
                      ETHYLBUTYL)UREA/CN
E10             1     N-(3,5-DICHLORO-2-HYDROXY-4-METHYLPHENYL)-N'-(2,6-DIMETHYLPH
                      ENYL)UREA/CN
E11             1     N-(3,5-DICHLORO-2-HYDROXY-4-METHYLPHENYL)-N'-(3,4,5-TRIMETHO
                      XYPHENYL)UREA/CN
E12             1     N-(3,5-DICHLORO-2-HYDROXY-4-METHYLPHENYL)-N'-(3,5-DICHLOROPH
                      ENYL)UREA/CN

=> S
N-(3,5-dichloro-1-oxo-pyridin-4-yl)-4-(difluoromethoxy)-3-cyclopropylmethoxybenzamid
e/cn
MISSING OPERATOR 'N-(3,5-DICHLO'

=> exp
N-(3,5-dichloro-1-oxo-pyridin-4-yl)-4-(difluoromethoxy)-3-cyclopropylmethoxybenzamid
e/cn
E1              1     N-(3,5-DICARBOXYPHENYL)MALEIMIDE/CN
E2              1     N-(3,5-DICARBOXYPHENYL)OCTADECYLAMIDE 1-HYDROXY-2-NAPHTHOIC
                      ACID/CN
E3              0 --> N-(3,5-DICHLORO-1-OXO-PYRIDIN-4-YL)-4-(DIFLUOROMETHOXY)-3-CY
                      CLOPROPYLMETHOXYBENZAMIDE/CN
E4              1     N-(3,5-DICHLORO-1-OXOPYRIDIN-4-YL)-2-(5-(4-FLUOROBENZYL)PYRR
                      OLO(2,1-B)THIAZOL-7-YL)-2-(OXO)ACETAMIDE/CN
E5              1     N-(3,5-DICHLORO-1-OXOPYRIDIN-4-YL)-2-(7-(4-FLUOROBENZYL)PYRR
                      OLO(1,2-B)PYRIDAZIN-5-YL)-2-(OXO)ACETAMIDE/CN
E6              1     N-(3,5-DICHLORO-1-OXOPYRIDIN-4-YL)-3-(6-(1-(METHANESULFONYL)
                      -1-METHYLETHYL)QUINOLIN-8-YL)BENZAMIDE/CN
E7              1     N-(3,5-DICHLORO-1-OXOPYRIDIN-4-YL)-4-DIFLUOROMETHOXY-3-CYCLO
                      PROPYLMETHOXYBENZAMIDE/CN
E8              1     N-(3,5-DICHLORO-2,6-DIFLUOROPYRID-4-YL)-3-CYCLOPENTYLOXY-4-M
                      ETHOXYBENZAMIDE/CN
E9              1     N-(3,5-DICHLORO-2-HYDROXY-4-METHYLPHENYL)-N'-(1,1,3,3-TETRAM
                      ETHYLBUTYL)UREA/CN
E10             1     N-(3,5-DICHLORO-2-HYDROXY-4-METHYLPHENYL)-N'-(2,6-DIMETHYLPH
                      ENYL)UREA/CN
E11             1     N-(3,5-DICHLORO-2-HYDROXY-4-METHYLPHENYL)-N'-(3,4,5-TRIMETHO
                      XYPHENYL)UREA/CN
E12             1     N-(3,5-DICHLORO-2-HYDROXY-4-METHYLPHENYL)-N'-(3,5-DICHLOROPH
                      ENYL)UREA/CN

=> log hold
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               1.44       1.66

 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 17:43:32 ON 05 FEB 2009

Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:SSPTAEXO1623

PASSWORD:
```

```
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'REGISTRY' AT 17:55:01 ON 05 FEB 2009
FILE 'REGISTRY' ENTERED AT 17:55:01 ON 05 FEB 2009
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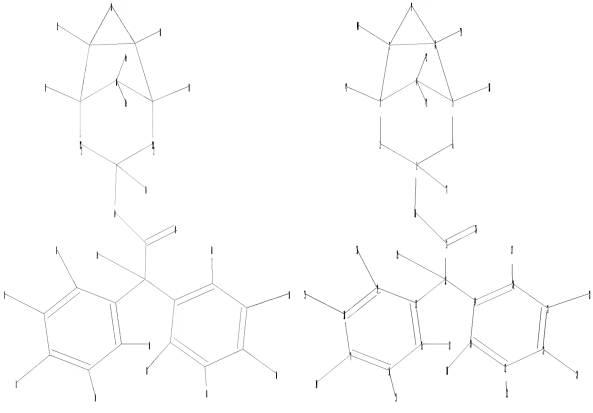
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     1.44       1.66

=>
Uploading C:\Program Files\STNEXP\Queries\10614365anticholinergic.str
```



```
chain nodes :
10  11  12  25  26  27  28  29  30  31  32  33  34  35  36  37  38  39  40  41  42
43
ring nodes :
1  2  3  4  5  6  7  8  9  13  14  15  16  17  18  19  20  21  22  23  24
chain bonds :
1-10  1-37  3-41  4-42  4-43  5-38  7-40  8-39  10-11  11-12  11-26  12-13  12-14
12-25  15-31  16-33  17-34  18-35  19-36  20-27  21-28  22-29  23-32  24-30
ring bonds :
1-2  1-6  2-3  3-4  3-7  4-5  5-6  5-8  7-8  7-9  8-9  13-15  13-19  14-20  14-24
15-16  16-17  17-18  18-19  20-21  21-22  22-23  23-24
exact/norm bonds :
1-2  1-6  1-10  2-3  3-4  3-7  4-5  5-6  5-8  7-8  7-9  8-9  10-11  11-26
exact bonds :
1-37  3-41  4-42  4-43  5-38  7-40  8-39  11-12  12-13  12-14  12-25  15-31  16-33
17-34  18-35  19-36  20-27  21-28  22-29  23-32  24-30
normalized bonds :
13-15  13-19  14-20  14-24  15-16  16-17  17-18  18-19  20-21  21-22  22-23  23-24
```

```
Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:CLASS
11:CLASS  12:CLASS  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:Atom
20:Atom  21:Atom
22:Atom  23:Atom  24:Atom  25:CLASS  26:CLASS  27:CLASS  28:CLASS  29:CLASS
30:CLASS  31:CLASS
32:CLASS  33:CLASS  34:CLASS  35:CLASS  36:CLASS  37:CLASS  38:CLASS  39:CLASS
40:CLASS  41:CLASS
42:CLASS  43:CLASS




=> log hold
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     1.92       2.14

 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 17:55:22 ON 05 FEB 2009

Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:SSPTAEXO1623

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  NOV 21  CAS patent coverage to include exemplified prophetic
                  substances identified in English-, French-, German-,
                  and Japanese-language basic patents from 2004-present
 NEWS  3  NOV 26  MARPAT enhanced with FSORT command
 NEWS  4  NOV 26  CHEMSAFE now available on STN Easy
 NEWS  5  NOV 26  Two new SET commands increase convenience of STN
                  searching
 NEWS  6  DEC 01  ChemPort single article sales feature unavailable
 NEWS  7  DEC 12  GBFULL now offers single source for full-text
                  coverage of complete UK patent families
 NEWS  8  DEC 17  Fifty-one pharmaceutical ingredients added to PS
 NEWS  9  JAN 06  The retention policy for unread STNmail messages
                  will change in 2009 for STN-Columbus and STN-Tokyo
 NEWS 10  JAN 07  WPIDS, WPINDEX, and WPIX enhanced Japanese Patent
                  Classification Data
 NEWS 11  FEB 02  Simultaneous left and right truncation (SLART) added
                  for CERAB, COMPUAB, ELCOM, and SOLIDSTATEM
 NEWS 12  FEB 02  GENBANK enhanced with SET PLURALS and SET SPELLING

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.
```

```
 NEWS HOURS     STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN     Welcome Banner and News Items
 NEWS IPC8      For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 09:10:50 ON 06 FEB 2009

=> file registry
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                          0.22       0.22

FILE 'REGISTRY' ENTERED AT 09:10:56 ON 06 FEB 2009
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STRUCTURE FILE UPDATES:    4 FEB 2009  HIGHEST RN 1100909-82-7
DICTIONARY FILE UPDATES:   4 FEB 2009  HIGHEST RN 1100909-82-7

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TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\STNEXP\Queries\10614365anticholinergic.str
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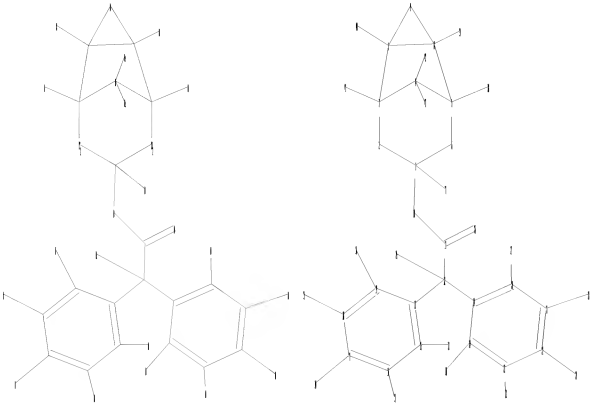


chain nodes :
10 11 12 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42
43
ring nodes :
1 2 3 4 5 6 7 8 9 13 14 15 16 17 18 19 20 21 22 23 24
chain bonds :
1-10 1-37 3-41 4-42 4-43 5-38 7-40 8-39 10-11 11-12 11-26 12-13 12-14
12-25 15-31 16-33 17-34 18-35 19-36 20-27 21-28 22-29 23-32 24-30
ring bonds :
1-2 1-6 2-3 3-4 3-7 4-5 5-6 5-8 7-8 7-9 8-9 13-15 13-19 14-20 14-24
15-16 16-17 17-18 18-19 20-21 21-22 22-23 23-24
exact/norm bonds :
1-2 1-6 1-10 2-3 3-4 3-7 4-5 5-6 5-8 7-8 7-9 8-9 10-11 11-26
exact bonds :
1-37 3-41 4-42 4-43 5-38 7-40 8-39 11-12 12-13 12-14 12-25 15-31 16-33
17-34 18-35 19-36 20-27 21-28 22-29 23-32 24-30
normalized bonds :
13-15 13-19 14-20 14-24 15-16 16-17 17-18 18-19 20-21 21-22 22-23 23-24

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom
22:Atom 23:Atom 24:Atom 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS
30:CLASS 31:CLASS
32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS
40:CLASS 41:CLASS
42:CLASS 43:CLASS

```
L1      STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 09:11:21 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        2 TO ITERATE

100.0% PROCESSED        2 ITERATIONS                                1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:             2 TO       124
PROJECTED ANSWERS:                1 TO        80

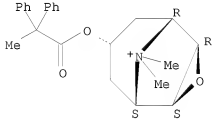
L2            1 SEA SSS SAM L1

=> d l2 scan


L2   1 ANSWERS   REGISTRY  COPYRIGHT 2009 ACS on STN
IN   3-Oxa-9-azoniatricyclo[3.3.1.02,4]nonane,
     9,9-dimethyl-7-(1-oxo-2,2-diphenylpropoxy)-,
     (1α,2β,4β,5α,7β)-, (2E)-2-butenedioate (1:1)
     (9CI)
MF   C24 H28 N O3 . C4 H3 O4

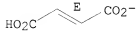
     CM   1

Relative stereochemistry.
```




```
     CM   2

Double bond geometry as shown.
```




```
ALL ANSWERS HAVE BEEN SCANNED

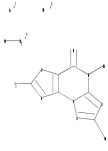

=> s l1 sss full
FULL SEARCH INITIATED 09:11:37 FILE 'REGISTRY'
```

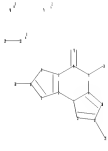
FULL SCREEN SEARCH COMPLETED - 42 TO ITERATE

100.0% PROCESSED 42 ITERATIONS 33 ANSWERS
SEARCH TIME: 00.00.01

L3 33 SEA SSS FUL L1

=>
Uploading C:\Program Files\STNEXP\Queries\10614365pde4.str





chain nodes :
13 14 15 21 22 23 25 27
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
4-13 5-25 8-21 11-27 22-23
ring bonds :
1-2 1-6 1-12 2-3 2-7 3-4 3-9 4-5 5-6 6-10 7-8 8-9 10-11 11-12
exact/norm bonds :

```
1-2  1-6  1-12  2-3  2-7  3-4  3-9  4-5  4-13  5-6  5-25  6-10  7-8  8-9  8-21
10-11
11-12  11-27
exact bonds :
22-23


G1:Ph,[*1],[*2],[*3]

Connectivity :
14:1 X maximum RC ring/chain  15:1 X maximum RC ring/chain  25:1 X maximum RC
ring/chain

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:CLASS  14:Atom  15:CLASS  21:CLASS  22:CLASS  23:CLASS
25:CLASS  27:CLASS
Generic attributes :
14:
Number of Carbon Atoms : less than 7
Type of Ring System    : Monocyclic
15:
Saturation             : Saturated
Number of Carbon Atoms : less than 7
25:
Number of Carbon Atoms : less than 7
27:
Saturation             : Saturated

Element Count :
Node 14: Limited
    N,N0-2
    C,C3-6
    O,O0-2
    S,S0

Node 25: Limited
    C,C1-5

Node 27: Limited
    C,C1-5




L4      STRUCTURE UPLOADED

=> s l4
SAMPLE SEARCH INITIATED 09:11:58 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       28 TO ITERATE

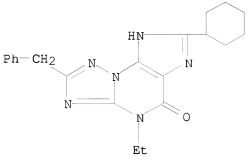
100.0% PROCESSED       28 ITERATIONS                                2 ANSWERS
SEARCH TIME: 00.00.02

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:          243 TO      877
PROJECTED ANSWERS:               2 TO      124
```

```
L5             2 SEA SSS SAM L4

=> d 15 scan

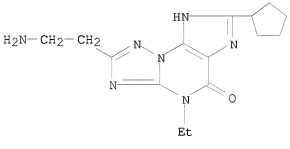
L5   2 ANSWERS   REGISTRY  COPYRIGHT 2009 ACS on STN
IN   5H-[1,2,4]Triazolo[5,1-b]purin-5-one,
     7-cyclohexyl-4-ethyl-4,8-dihydro-2-(phenylmethyl)-
MF   C21 H24 N6 O
```




```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**


HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L5   2 ANSWERS   REGISTRY  COPYRIGHT 2009 ACS on STN
IN   5H-[1,2,4]Triazolo[5,1-b]purin-5-one,
     2-(2-aminoethyl)-7-cyclopentyl-4-ethyl-4,8-dihydro-
MF   C15 H21 N7 O
```

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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**


ALL ANSWERS HAVE BEEN SCANNED


=> s l4 sss full
FULL SEARCH INITIATED 09:12:15 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -       561 TO ITERATE

100.0% PROCESSED       561 ITERATIONS                                91 ANSWERS
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SEARCH TIME: 00.00.01

L6 91 SEA SSS FUL L4

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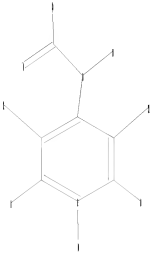

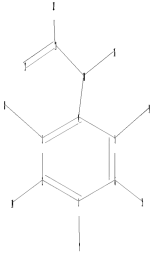

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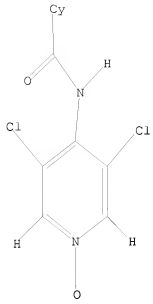
7 8 9 10 11 12 13 14 15 16
ring nodes :
1 2 3 4 5 6
chain bonds :
1-7 2-14 3-8 4-10 5-9 6-15 10-11 10-16 11-12 11-13
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-7 4-10 10-11 11-12 11-13
exact bonds :
2-14 3-8 5-9 6-15 10-16
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS

L7 STRUCTURE UPLOADED

=> d l7
L7 HAS NO ANSWERS
L7 STR



Structure attributes must be viewed using STN Express query preparation.

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=> s l7
SAMPLE SEARCH INITIATED 09:12:38 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       31 TO ITERATE

100.0% PROCESSED       31 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          286 TO      954
PROJECTED ANSWERS:               0 TO        0

L8            0 SEA SSS SAM L7

=> s l7 sss full
FULL SEARCH INITIATED 09:12:44 FILE 'REGISTRY'
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100.0% PROCESSED      572 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

L9            0 SEA SSS FUL L7

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Uploading C:\Program Files\STNEXP\Queries\10614365pde4c.str
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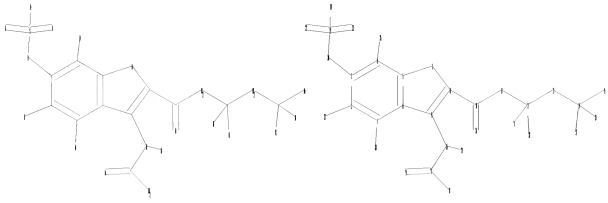

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31 32 33
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
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14-15 14-30 14-33 16-17 16-29 17-18 17-19 20-21 21-22 21-23 21-24
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9
exact/norm bonds :
3-20 5-7 6-9 7-8 8-9 9-16 10-25 16-17 17-18 17-19 20-21 21-22 21-23

exact bonds :
1-28 2-27 4-26 8-10 10-11 11-12 12-13 12-31 12-32 13-14 14-15 14-30
14-33
16-29 21-24
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS
21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS
29:CLASS 30:CLASS
31:CLASS 32:CLASS 33:CLASS

L10 STRUCTURE UPLOADED

=> s l10 fam full
FULL SEARCH INITIATED 09:13:06 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

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L11            0 SEA FAM FUL L10

=> d l10
L10 HAS NO ANSWERS
L10              STR
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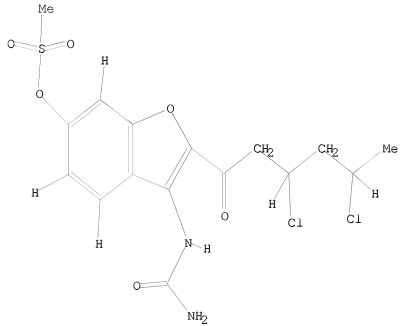

Structure attributes must be viewed using STN Express query preparation.

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=> s roflumilast/cn
L12            1 ROFLUMILAST/CN

=> s theophylline/cn
L13            1 THEOPHYLLINE/CN

=> s tofimilast/cn
L14            1 TOFIMILAST/CN

=> s pumafentrine/cn
L15            1 PUMAFENTRINE/CN

=> d his

     (FILE 'HOME' ENTERED AT 09:10:50 ON 06 FEB 2009)

     FILE 'REGISTRY' ENTERED AT 09:10:56 ON 06 FEB 2009
L1               STRUCTURE UPLOADED
L2             1 S L1
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L4               STRUCTURE UPLOADED
L5             2 S L4
L6            91 S L4 SSS FULL
L7               STRUCTURE UPLOADED
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L8             0 S L7
L9             0 S L7 SSS FULL
L10              STRUCTURE UPLOADED
L11            0 S L10 FAM FULL
L12            1 S ROFLUMILAST/CN
L13            1 S THEOPHYLLINE/CN
L14            1 S TOFIMILAST/CN
L15            1 S PUMAFENTRINE/CN

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             652.85     653.07

FILE 'HCAPLUS' ENTERED AT 09:14:09 ON 06 FEB 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 6 Feb 2009  VOL 150 ISS 7
FILE LAST UPDATED: 5 Feb 2009  (20090205/ED)

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.
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This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l3 sss full
L16           38 L3

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              6 L6/THU
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             31 L14
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                (L14 (L) THU/RL)
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        1091697 THU/RL
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                (L12 (L) THU/RL)
           34 L15
      1091697 THU/RL
           34 L15/THU
                (L15 (L) THU/RL)
L17       3374 L6/THU OR L13/THU OR L14/THU OR L12/THU OR L15/THU

=> s l16 and l17
L18          2 L16 AND L17

=> d l18 1-2 ti abs bib

L18  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   New pharmaceutical compositions for treatment of respiratory and
     gastrointestinal disorders
AB   The present invention relates to novel pharmaceutical compns. comprising
     at least one EGFR kinase inhibitor and at least one addnl. active compound
     selected from beta-2 mimetics, steroids, PDE-IV inhibitors, p38 MAP kinase
     inhibitors, NK1 antagonists, anticholinergics and endothelin antagonists,
     processes for preparing the compns. and the use thereof as medicament in the
     treatment of respiratory or gastrointestinal complaints, as well as
     inflammatory diseases of the joints, the skin or the eyes.
AN   2008:529495  HCAPLUS <<LOGINID::20090206>>
DN   148:509924
TI   New pharmaceutical compositions for treatment of respiratory and
     gastrointestinal disorders
IN   Jung, Birgit; Himmelsbach, Frank; Pohl, Gerald
PA   Boehringer Ingelheim International GmbH, Germany; Boehringer Ingelheim
     Pharma Gmbh & Co.Kg
SO   PCT Int. Appl., 96pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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PI   WO 2008049842       A2     20080502    WO 2007-EP61355        20071023
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              CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI,
              GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
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              PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
              TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
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              BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
PRAI US 2006-862990P      P      20061026

L18  ANSWER 2 OF 2  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Pharmaceutical compositions comprising anticholinergic agents and
     phosphodiesterase IV (PDE-IV) inhibitors for the treatment of respiratory
     diseases
AB   The invention provides pharmaceutical compns. comprising anticholinergic
     agents and PDE-IV inhibitors, as well as a method for the production and use
     thereof in the treatment of respiratory diseases.  Powder inhalant
     formulations are included.
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AN 2004:41257 HCAPLUS <<LOGINID::20090206>>
DN 140:87709
TI Pharmaceutical compositions comprising anticholinergic agents and phosphodiesterase IV (PDE-IV) inhibitors for the treatment of respiratory diseases
IN Pairet, Michel; Meade, Christopher John Montague; Pieper, Michael P.
PA Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SO PCT Int. Appl., 37 pp.
    CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

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	DE 10230769	A1	20040122	DE 2002-10230769	20020709
	CA 2492026	A1	20040115	CA 2003-2492026	20030625
	AU 2003242755	A1	20040123	AU 2003-242755	20030625
	EP 1521576	A1	20050413	EP 2003-762509	20030625
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005532379	T	20051027	JP 2004-518566	20030625
	US 20040058950	A1	20040325	US 2003-614365	20030707
PRAI	DE 2002-10230769	A	20020709		
	US 2002-407895P	P	20020903		
	WO 2003-EP6668	W	20030625		

OS MARPAT 140:87709
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
           ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s l16 and l19
L20         31 L16 AND L19

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L21          9 L20 AND (PY<2003 OR AY<2003 OR PRY<2003)

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           328 PDE 4
               (PDE(W)4)
          6075 PDE
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           549 PDE IV
                 (PDE(W)IV)
         29000 PHOSPHODIESTERASE
       6074473 4
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          1901 PHOSPHODIESTERASE(W)(4 OR IV)
L22       3212 PDE4 OR PDEIV OR (PDE 4) OR (PDE IV) OR (PHOSPHODIESTERASE(W)(4
               OR IV))

=> l17 and l22
L17 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l17 and l22
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L24          78 L23 AND (PY<2002 OR AY<2002 OR PRY<2002)

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MISSING OPERATOR L19 ADN
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nested terms that are not separated by a logical operator.

=> s l19 and l24
L25           3 L19 AND L24

=> d l25 1-3 ti abs bib

L25  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Pharmaceutical compositions based on anticholinergics and additional
     active ingredients
AB   A pharmaceutical composition comprising an anticholinergic and at
     least one addnl. active ingredient selected from among corticosteroids,
     dopamine agonists, PDE-IV inhibitors, NK1-antagonists,
     endothelin antagonists, antihistamines, and EGFR-kinase inhibitors,
     processes for preparing them and their use in the treatment of respiratory
     diseases.  Among a number of compds. prepared was
     N-[2-[3,5-bis(trifluoromethyl)phenyl]ethyl]-2-[4-[(3-
     hydroxypropyl)methylamino]piperidin-1-yl]-N-methyl-2-phenylacetamide.
     Inhalable powders include a formulation containing tiotropium bromide,
     budesonide, and lactose.
AN   2005:586215  HCAPLUS <<LOGINID::20090206>>
DN   143:120526
TI   Pharmaceutical compositions based on anticholinergics and additional
     active ingredients
IN   Pairet, Michel; Pieper, Michael P.; Meade, Christopher John Montague;
     Reichl, Richard; Schmelzer, Christel; Jung, Birgit
PA   Boehringer Ingelheim Pharma GmbH & Co. Kg, Germany
SO   U.S. Pat. Appl. Publ., 50 pp., Cont.-in-part of U.S. Ser. No. 824,391.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 19
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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OS MARPAT 143:120526

L25 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Pharmaceutical compositions based on anticholinergics and PDE-IV inhibitors

AB The present invention relates to novel pharmaceutical compns. based on anticholinergics and phosphodiesterase (PDE) IV inhibitors, processes for preparing them and their use in the treatment of respiratory tract diseases. For example, a suspension aerosol contained tiotropium bromide 0.029%, AWD 12-281 0.033%, ethanol 0.5%, iso-Pr myristate 0.1%, and TG 227 to 100%.

AN 2002:965129 HCAPLUS <<LOGINID::20090206>>

DN 138:44711

TI Pharmaceutical compositions based on anticholinergics and PDE-IV inhibitors

IN Pairet, Michel; Meade, Christopher J. M.; Pieper, Michael P.

PA Germany

SO U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Provisional Ser. No. 281,857.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 19

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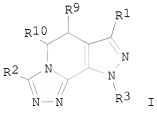
	US 2004-775901	A2	20040210
	US 2004-776757	A2	20040211
	US 2004-824391	A2	20040414
	AU 2006-202723	A3	20060626

OS MARPAT 138:44711

L25 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2009 ACS on STN
TI A PDE 4 inhibitor and an anti-cholinergic agent in combination for treating obstructive airways diseases
GI



I

AB The present invention discusses combination of a selective PDE4 inhibitor I [R1 = H, (C1-6) alkyl, alkoxy, Ph cycloalkyl etc.; R2, R3 = H, (C1-14) alkyl, (C2-14)alkenyl, (C1-7)alkoxy etc.; R9, R10 = (C1-6) alkyl, alkoxy, (C6-10)aryl and aryloxy] and an anticholinergic agent for simultaneous, sequential or sep. administration by the inhaled route in the treatment of an obstructive airways or other inflammatory disease, with the proviso that the anticholinergic agent is not a tiotropium salt.

AN 2002:927276 HCAPLUS <<LOGINID::20090206>>
DN 138:11421
TI A PDE 4 inhibitor and an anti-cholinergic agent in combination for treating obstructive airways diseases
IN Yeadon, Michael; Watson, John W.; Armstrong, Roisin A.
PA Pfizer Inc., USA
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002096463	A1	20021205	WO 2002-EP5726	20020524 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2446613	A1	20021205	CA 2002-2446613	20020524 <--
AU 2002344167	A1	20021209	AU 2002-344167	20020524 <--
EP 1395288	A1	20040310	EP 2002-750977	20020524 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

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     BR 2002009992          A     20040406    BR 2002-9992           20020524 <--
     EE 200300585           A     20040415    EE 2003-585            20020524 <--
     HU 2004000037          A2    20040428    HU 2004-37             20020524 <--
     CN 1511042             A     20040707    CN 2002-810498         20020524 <--
     JP 2005508861          T     20050407    JP 2002-592972         20020524 <--
     NZ 529335              A     20050930    NZ 2002-529335         20020524 <--
     ZA 2003008602          A     20050204    ZA 2003-8602           20031104 <--
     MX 2003010162          A     20040310    MX 2003-10162          20031106 <--
     IN 2003MN01033         A     20051021    IN 2003-MN1033         20031111 <--
     US 20040147544         A1    20040729    US 2003-478755         20031121
     BG 108382              A     20041230    BG 2003-108382         20031124 <--
PRAI US 2001-293606P        P     20010525  <--
     GB 2001-29396          A     20011207  <--
     GB 2002-10240          A     20020503
     WO 2002-EP5726         W     20020524
OS   MARPAT 138:11421
RE.CNT  3     THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> s inflamm? or asthma or COPD
        339408 INFLAMM?
         42742 ASTHMA
          4525 COPD
L26     365584 INFLAMM? OR ASTHMA OR COPD

=> s l24 and l26
L27          48 L24 AND L26

=> d l27 1-48 ti abs bib

L27  ANSWER 1 OF 48  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Synergistic combination
AB   The invention relates to the combined administration of PDE inhibitors,
     such as roflumilast, and β2 adrenoceptor agonists for the treatment
     of respiratory tract disorders.
AN   2003:749998  HCAPLUS <<LOGINID::20090206>>
DN   139:255370
TI   Synergistic combination
IN   Kilian, Ulrich; Schudt, Christian
PA   Altana Pharma A.-G., Germany
SO   U.S., 29 pp., Cont.-in-part of U. S. Ser. No. 367,850.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 3
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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PI   US 6624181           B1    20030923    US 2002-49999          20020220 <--
     WO 9837894           A1    19980903    WO 1998-EP1047         19980224 <--
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             LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, VN, YU, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     US 6333354           B1    20011225    US 1999-367850         19990827 <--
     WO 2001013953        A2    20010301    WO 2000-EP7852         20000811 <--
     WO 2001013953        A3    20010920
         W:  AE, AL, AU, BA, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN,
             JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
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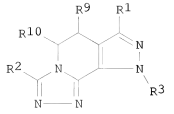
PT, SE
EP 1671651 A1 20060621 EP 2006-110822 20000811 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
US 20040034087 A1 20040219 US 2003-437005 20030514 <--
US 7056936 B2 20060606
US 20060079539 A1 20060413 US 2005-286391 20051125 <--
US 20060205806 A1 20060914 US 2006-433419 20060515 <--
PRAI DE 1997-19708049 A 19970228 <--
WO 1998-EP1047 W 19980224 <--
EP 1999-116447 A 19990821 <--
US 1999-367850 A2 19990827 <--
WO 2000-EP7852 W 20000811 <--
EP 2000-954625 A3 20000811 <--
US 2002-49999 A1 20020220
US 2003-437005 A1 20030514
US 2005-286391 A1 20051125
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Combinations of a cyclooxygenase-2 selective inhibitor and a TNF-α antagonist and therapeutic uses therefor
AB A method for the prevention, treatment, or inhibition of pain, inflammation, or inflammation-related disorder and for the prevention, treatment, or inhibition of a cardiovascular disease or disorder in a subject that is in need of such prevention, treatment or inhibition, involves the administration to the subject of a cyclooxygenase-2 selective inhibitor or prodrug thereof and a TNF-α antagonist. A method can also involve the treatment, prevention, or inhibition of cancer in a subject in need of such treatment, prevention, or inhibition, by administering to the subject a cyclooxygenase-2 selective inhibitor or prodrug thereof and a TNF-α antagonist which is selected from the group consisting of a compound that affects the synthesis of TNF-α, a compound that inhibits the binding of TNF-α with a receptor specific for TNF-α, and a compound that interferes with intracellular signaling triggered by TNF-α binding with a receptor. Compns., pharmaceutical compns. and kits that can be used with the methods are also described.
AN 2003:656204 HCAPLUS <<LOGINID::20090206>>
DN 139:191422
TI Combinations of a cyclooxygenase-2 selective inhibitor and a TNF-α antagonist and therapeutic uses therefor
IN Bennett, Dennis A.
PA Pharmacia Corporation, USA
SO U.S. Pat. Appl. Publ., 39 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20030157061	A1	20030821	US 2002-310454	20021205 <--
PRAI	US 2001-337802P	P	20011205 <--		

L27 ANSWER 3 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Combination of a selective PDE4 inhibitor and an adrenergic β-2 receptor agonist in treatment of inflammatory diseases
GI



I

AB The present invention relates to a combination of a selective PDE4 inhibitor, as defined herein, and an adrenergic β-2 receptor agonist for simultaneous, sequential or sep. administration by the inhaled route in the treatment of an obstructive airways or other inflammatory disease. Combined application of β-2 agonists such as formoterol or salmeterol with a PDE-4 inhibitor such as I produces synergistic inhibition of proinflammatory neutrophil function.

AN 2003:454118 HCAPLUS <<LOGINID::20090206>>

DN 139:17580

TI Combination of a selective PDE4 inhibitor and an adrenergic β-2 receptor agonist in treatment of inflammatory diseases

IN Yeadon, Michael

PA Pfizer Limited, UK; Pfizer Inc.

SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003047578	A1	20030612	WO 2002-IB4922	20021122 <--
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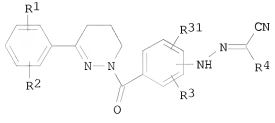
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2468676	A1	20030612	CA 2002-2468676	20021122 <--
	AU 2002353255	A1	20030617	AU 2002-353255	20021122 <--
	EP 1455783	A1	20040915	EP 2002-788275	20021122 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	BR 2002014776	A	20041109	BR 2002-14776	20021122 <--
	CN 1599609	A	20050323	CN 2002-824393	20021122 <--
	HU 2004002546	A2	20050428	HU 2004-2546	20021122 <--
	HU 2004002546	A3	20080428		
	JP 2005511657	T	20050428	JP 2003-548833	20021122 <--
	NZ 533030	A	20070330	NZ 2002-533030	20021122 <--
	US 20030119862	A1	20030626	US 2002-308962	20021203 <--
	TW 242433	B	20051101	TW 2002-91135479	20021206 <--
	US 20040167153	A1	20040826	US 2003-736996	20031216 <--
	ZA 2004003905	A	20050622	ZA 2004-3905	20040520 <--
	MX 2004004930	A	20050408	MX 2004-4930	20040524 <--
	NO 2004002870	A	20040706	NO 2004-2870	20040706 <--
	IN 2004DN01375	A	20050401	IN 2004-DN1375	20041121 <--

PRAI GB 2001-29395 A 20011207 <--
US 2002-352388P P 20020128
WO 2002-IB4922 W 20021122
OS MARPAT 139:17580
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 4 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Preparation of pyridazinylmethanoylphenylhydrazonomalonitriles as phosphodiesterase IV inhibitors.
GI



I

AB Title compds. [I; R1, R2 = H, OH, OR5, SR5, SOR5, SO2R5, X; R1R2 = OCH2O, OCH2CH2O; R3, R31 = H, R5, OH, OR5, NH2, NHR5, NHCOR5, X, CO2H, CO2R5, CONH2, etc.; R4 = cyano, tetrazolyl; R5 = (fluoro-substituted) A, cycloalkyl, (CH2)nAr; A = (fluoro- and/or chloro-substituted) alkyl, alkenyl; Ar = Ph; n = 0-2; X = F, Cl, Br, iodo], were prepared Thus, [3-(3,4-diethoxyphenyl)-5,6-dihydro-4H-pyridazine-1-yl]-(3-aminophenyl)methanone (preparation given) was stirred with NaNO2 in aqueous HCl for 1 h at -2° to 0°; malononitrile in H2O was added followed by stirring for 2 h to give a residue which was treated with KOH in MeOH to give 2-[[3-[1-[3-(3,4-diethoxyphenyl)-5,6-dihydro-4H-pyridazin-1-yl]methanoyl]phenyl]hydrazono]malononitrile K salt. I were said to give a marked reduction of T cell proliferation. I are claimed for treatment of osteoporosis, tumors, cachexia, atherosclerosis, rheumatoid arthritis, multiple sclerosis, diabetes mellitus, inflammatory processes, allergies, asthma, autoimmune diseases, myocardial diseases, AIDS, etc.
AN 2003:376641 HCAPLUS <<LOGINID::20090206>>
DN 138:385438
TI Preparation of pyridazinylmethanoylphenylhydrazonomalonitriles as phosphodiesterase IV inhibitors.
IN Eggenweiler, Hans-Michael; Wolf, Michael; Beier, Norbert; Schelling, Pierre; Ehring, Thomas
PA Merck Patent Gmbh, Germany
SO PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003039548	A1	20030515	WO 2002-EP11351	20021010 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,				

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            PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
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            PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
            NE, SN, TD, TG
    CA 2465746          A1   20030515    CA 2002-2465746         20021010 <--
    AU 2002363368       A1   20030519    AU 2002-363368          20021010 <--
    AU 2002363368       B2   20071213
    AU 2002363368       B9   20080124
    EP 1441730          A1   20040804    EP 2002-802625          20021010 <--
    EP 1441730          B1   20060809
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
    BR 2002013683       A    20041026    BR 2002-13683           20021010 <--
    HU 2004001747       A2   20050128    HU 2004-1747            20021010 <--
    HU 2004001747       A3   20050628
    CN 1585641          A    20050223    CN 2002-822216          20021010 <--
    JP 2005511595       T    20050428    JP 2003-541839          20021010 <--
    AT 335486           T    20060915    AT 2002-802625          20021010 <--
    ES 2268157          T3   20070316    ES 2002-802625          20021010 <--
    RU 2302412          C2   20070710    RU 2004-117171          20021010 <--
    MX 2004004263       A    20040708    MX 2004-4263            20040504 <--
    US 20040261190      A1   20041230    US 2004-494631          20040504 <--
    US 7141572          B2   20061128
    ZA 2004004387       A    20060222    ZA 2004-4387            20040603 <--
    US 20060270676      A1   20061130    US 2006-497235          20060802 <--
PRAI EP 2001-125455     A    20011105  <--
    WO 2002-EP11351     W    20021010
    US 2004-494631      A1   20040504
OS  MARPAT 138:385438
RE.CNT  4     THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27  ANSWER 5 OF 48  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Type 4 phosphodiesterase inhibitors and therapeutic uses thereof
AB   The invention discloses the use of type 4 phosphodiesterase inhibitors (
     PDE IV inhibitors) to treat diseases, as well as
     combinations of PDE IV inhibitors with other drugs.
AN   2003:356269  HCAPLUS <<LOGINID::20090206>>
DN   138:348761
TI   Type 4 phosphodiesterase inhibitors and therapeutic uses thereof
IN   Eggenweiler, Hans-Michael; Wolf, Michael
PA   Merck Patent G.m.b.H., Germany
SO   PCT Int. Appl., 122 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
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PI   WO 2003037349       A1     20030508    WO 2002-EP9596          20020828 <--
        W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
            FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
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     CA 2462525          A1    20030508    CA 2002-2462525        20020828 <--
     AU 2002333730       A1    20030512    AU 2002-333730         20020828 <--
     EP 1463509          A1    20041006    EP 2002-802281         20020828 <--
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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     CN 1578665          A     20050209    CN 2002-821711         20020828 <--
     HU 2004001984       A2    20050228    HU 2004-1984           20020828 <--
     HU 2004001984       A3    20050628
     JP 2005515975       T     20050602    JP 2003-539692         20020828 <--
     MX 2004003668       A     20040722    MX 2004-3668           20040419 <--
     US 20040259863      A1    20041223    US 2004-494379         20040430 <--
PRAI EP 2001-125394      A     20011031  <--
     WO 2002-EP9596      W     20020828
OS   MARPAT 138:348761
RE.CNT  14    THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27  ANSWER 6 OF 48  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Combination of phosphodiesterase 4 inhibitor and
     nonsteroidal antiinflammatory drug in treatment of inflammation
AB   The invention relates to the combined administration of PDE4
     -inhibitors and NSAIDs for the treatment of an inflammatory
     disease and/or an inflammation associated disorder while minimizing
     gastrointestinal side effects, such as gastric erosions and ulcer, which
     are frequently associated with the use of NSAIDs.  PDE4 inhibitors
     Rolipram, Roflumilast, and RP73401 inhibited or prevented diclofenac
     induced gastrointestinal bleeding in mice.
AN   2003:242192  HCAPLUS <<LOGINID::20090206>>
DN   138:248511
TI   Combination of phosphodiesterase 4 inhibitor and
     nonsteroidal antiinflammatory drug in treatment of inflammation
IN   Hatzelmann, Armin; Eltze, Manfrid; Klein, Thomas; Kley, Hans-Peter
PA   Altana Pharma A.-G., Germany
SO   PCT Int. Appl., 42 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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PI   WO 2003024489       A2     20030327    WO 2002-EP10424        20020917 <--
     WO 2003024489       A3     20030918
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             IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI,
             TN, UA, US, VN, YU, ZA, ZW
         RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
             DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR
     CA 2459757          A1     20030327    CA 2002-2459757        20020917 <--
     AU 2002337105       A1     20030401    AU 2002-337105         20020917 <--
     AU 2002337105       B2     20080320
     EP 1429807          A2     20040623    EP 2002-772313         20020917 <--
     EP 1429807          B1     20070228
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
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     HU 2004001582       A2     20041129    HU 2004-1582           20020917 <--
     HU 2004001582       A3     20080428
     JP 2005504077       T      20050210    JP 2003-528583         20020917 <--
     CN 1625411          A      20050608    CN 2002-818241         20020917 <--
     NZ 532278           A      20060224    NZ 2002-532278         20020917 <--
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	AT 355080	T	20060315	AT 2002-772313	20020917 <--
	ES 2282469	T3	20071016	ES 2002-772313	20020917 <--
	IN 2004MN00112	A	20050218	IN 2004-MN112	20040213 <--
	MX 2004002562	A	20040531	MX 2004-2562	20040318 <--
	US 20040242597	A1	20041202	US 2004-489920	20040318 <--
	ZA 2004002654	A	20050214	ZA 2004-2654	20040405 <--
	NO 2004001596	A	20040618	NO 2004-1596	20040419 <--
	HK 1066730	A1	20070824	HK 2004-109770	20041209 <--
	US 20080255209	A1	20081016	US 2007-3129	20071220 <--
PRAI	EP 2001-473	A	20010919 <--		
	WO 2002-EP10424	W	20020917		
	US 2004-489920	B3	20040318		

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 7 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Composition comprising a PDE-4 inhibitor and H1-receptor antagonist for treatment of respiratory diseases
AB A method of prophylaxis, treating, or reducing the duration or frequency of the exacerbations associated with a respiratory disease, such as chronic obstructive pulmonary disease or asthma, comprises administering to a patient an effective amount of a phosphodiesterase-4 (PDE-4) inhibitor, e.g., cilomilastat, in combination with an H1-receptor antagonist, e.g., loratadine. For example, a metered dose inhaler (e.g., for 120 actuations) was prepared containing cilomilast 18 mg, loratadine 12 mg, and 1,1,1,2-tetrafluoroethane to 75.0 mg.
AN 2003:5806 HCAPLUS <<LOGINID::20090206>>
DN 138:78456
TI Composition comprising a PDE-4 inhibitor and H1-receptor antagonist for treatment of respiratory diseases
IN Knowles, Richard Graham; Ward, Peter; Nials, Anthony Terence
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003000289	A1	20030103	WO 2002-GB2679	20020617 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2450758	A1	20030103	CA 2002-2450758	20020617 <--
	AU 2002310620	A1	20030108	AU 2002-310620	20020617 <--
	EP 1404369	A1	20040407	EP 2002-735611	20020617 <--
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	HU 2004000222	A2	20040728	HU 2004-222	20020617 <--
	HU 2004000222	A3	20060228		
	CN 1518460	A	20040804	CN 2002-812473	20020617 <--
	BR 2002010473	A	20040810	BR 2002-10473	20020617 <--
	JP 2005501023	T	20050113	JP 2003-506932	20020617 <--
	US 20040176419	A1	20040909	US 2003-480969	20031208 <--
	IN 2003DN02141	A	20060120	IN 2003-DN2141	20031209 <--

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     ZA 2003009587        A     20050117    ZA 2003-9587           20031210 <--
     MX 2003011702        A     20040319    MX 2003-11702          20031216 <--
PRAI GB 2001-15181        A     20010620  <--
     WO 2002-GB2679       W     20020617
RE.CNT  5     THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27  ANSWER 8 OF 48  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   A PDE 4 inhibitor and an anti-cholinergic agent in
     combination for treating obstructive airways diseases
GI
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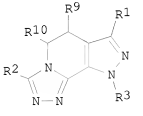

I


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AB   The present invention discusses combination of a selective PDE4
     inhibitor I [R1 = H, (C1-6) alkyl, alkoxy, Ph cycloalkyl etc.; R2, R3 = H,
     (C1-14) alkyl, (C2-14)alkenyl, (C1-7)alkoxy etc.; R9, R10 = (C1-6) alkyl,
     alkoxy, (C6-10)aryl and aryloxy] and an anticholinergic agent for
     simultaneous, sequential or sep. administration by the inhaled route in
     the treatment of an obstructive airways or other inflammatory
     disease, with the proviso that the anticholinergic agent is not a
     tiotropium salt.
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AN   2002:927276  HCAPLUS <<LOGINID::20090206>>
DN   138:11421
TI   A PDE 4 inhibitor and an anti-cholinergic agent in
     combination for treating obstructive airways diseases
IN   Yeadon, Michael; Watson, John W.; Armstrong, Roisin A.
PA   Pfizer Inc., USA
SO   PCT Int. Appl., 34 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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PI   WO 2002096463        A1    20021205    WO 2002-EP5726         20020524 <--
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2446613            A1    20021205    CA 2002-2446613        20020524 <--
     AU 2002344167         A1    20021209    AU 2002-344167         20020524 <--
     EP 1395288            A1    20040310    EP 2002-750977         20020524 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
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     BR 2002009992          A      20040406    BR 2002-9992           20020524 <--
     EE 200300585           A      20040415    EE 2003-585            20020524 <--
     HU 2004000037          A2     20040428    HU 2004-37             20020524 <--
     CN 1511042             A      20040707    CN 2002-810498         20020524 <--
     JP 2005508861          T      20050407    JP 2002-592972         20020524 <--
     NZ 529335              A      20050930    NZ 2002-529335         20020524 <--
     ZA 2003008602          A      20050204    ZA 2003-8602           20031104 <--
     MX 2003010162          A      20040310    MX 2003-10162          20031106 <--
     IN 2003MN01033         A      20051021    IN 2003-MN1033         20031111 <--
     US 20040147544         A1     20040729    US 2003-478755         20031121
     BG 108382              A      20041230    BG 2003-108382         20031124 <--
PRAI US 2001-293606P        P      20010525  <--
     GB 2001-29396          A      20011207  <--
     GB 2002-10240          A      20020503
     WO 2002-EP5726         W      20020524
OS   MARPAT 138:11421
RE.CNT  3      THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27  ANSWER 9 OF 48  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Combination of a PDE4 inhibitor and tiotropium for treating
     obstructive airways and other inflammatory diseases
AB   The present invention relates to a combination of therapeutic agents
     useful in the treatment of obstructive airways and other
     inflammatory diseases comprising a PDEIV inhibitor that
     is effective in the treatment of the above diseases when administered by
     inhalation together with an anti-cholinergic agent selected from the group
     consisting of tiotropium and derivs.  A method of treating the obstructive
     airways and other inflammatory diseases comprises administering
     by inhalation an effective amount of the above combination of agents and a
     package containing a composition for insertion into a device capable of
     simultaneous or sequential delivery of the pharmaceutical composition in the
     form of an aerosol or a dry powder dispersion to the mammal, where the
     device is a metered dose inhaler or a dry powder inhaler.  The
     anti-cholinergic agent component may be tiotropium bromide.  A package in
     the form of a pressurized, tetrafluoroethylene-coated aluminum canister
     for use in a metered dose inhaler is prepared which is sufficient to provide
     about 200 actuations of the inhaler, each actuation providing about 20
     μg each active ingredient.  The contents of each canister are as
     follows: 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-thienyl)-9H-pyrazolo[3,4-
     c]-1,2,4-triazolo[4,3-a]pyridine, tiotropium bromide,
     dichlorodifluoromethane, dichlorotetrafluoroethane,
     trichloromonofluoromethane, and soya lecithin.
AN   2002:927247  HCAPLUS <<LOGINID::20090206>>
DN   138:16606
TI   Combination of a PDE4 inhibitor and tiotropium for treating
     obstructive airways and other inflammatory diseases
IN   Yeadon, Michael; Armstrong, Roisin A.; Watson, John W.
PA   Boehringer Ingelheim Pharma KG, Germany
SO   PCT Int. Appl., 105 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    -------------------    --------
PI   WO 2002096423        A2    20021205    WO 2002-EP5643         20020523 <--
     WO 2002096423        A3    20030206
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2448363	A1	20021205	CA 2002-2448363	20020523	<--
AU 2002314102	A1	20021209	AU 2002-314102	20020523	<--
EP 1397135	A2	20040317	EP 2002-740638	20020523	<--
EP 1397135	B1	20061206			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004530705	T	20041007	JP 2002-592933	20020523	<--
AT 347361	T	20061215	AT 2002-740638	20020523	<--
ES 2276942	T3	20070701	ES 2002-740638	20020523	<--
US 20050107420	A1	20050519	US 2003-715177	20031117	
MX 2003010791	A	20040302	MX 2003-10791	20031125	<--
PRAI US 2001-293555P	P	20010525	<--		
US 2001-303845P	P	20010709	<--		
WO 2002-EP5643	W	20020523			

OS MARPAT 138:16606

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 10 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Preparation of pyrimidinylaminothiazolecarboxylates and related pyrimidines as dual inhibitors of phosphodiesterases PDE 7 and PDE 4

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Dual inhibitors of PDE 7 and PDE 4 (pyrimidines, e.g. I), together with their use to treat leukocyte activation-associated disorders (including transplant rejection, rheumatoid arthritis, inflammatory bowel disease, psoriasis, asthma, chronic obstructive pulmonary disease, lupus and multiple sclerosis), are provided herein. The present invention further provides for a method of reducing or alleviating nausea and emesis associated with the administration of PDE4 inhibitors comprising either the administration of a dual PDE 7-PDE 4 inhibitor, or the simultaneous or sequential co-administration of a selective PDE 7 inhibitor together with a selective PDE 4 inhibitor. In I, R1a is H or alkyl; R2a is optionally substituted heteroaryl; Z is halogen, alkyl, substituted alkyl, haloalkyl, or NR3aR4a; R3a is H or alkyl; R4a is alkyl, optionally substituted (heteroaryl)alkyl, optionally substituted heterocyclo, optionally substituted (heterocyclo)alkyl, or (aryl)alkyl wherein the aryl group is substituted with one or two groups T1* and T2* and optionally further substituted with a group T3*; or R3a and R4a together with the N atom to which they are attached may combine to form an optionally substituted heterocyclo ring; R5a is (aryl)alkyl wherein the aryl group is substituted with one or two groups T1* and T2* and optionally further substituted with a group T3*; R6a is H or alkyl; R7a is H or alkyl; T1* and T2* are independently alkoxy, alkoxycarbonyl, heteroaryl or -SO2R8a where R8a is alkyl, amino, alkylamino or dialkylamino; or T1* and T2* together with the atoms to which they are attached may combine to form a ring (e.g., benzodioxole); T3* is H, alkyl, halo, haloalkyl or cyano. Other pyrimidine classes (II-V) are described in the claims; this patent

differs from WO 02/088079 with regard to IV (J1 and J2 are same or different and are optionally substituted alkylene group of 1-3 C atoms, provided that they are not both greater than C2 alkylene). Pharmaceutical properties for 2-[[4-[4-(dimethylamino)-1-piperidinyl]-6-[[(3,4,5-trimethoxyphenyl)methyl]amino]-2-pyrimidinyl]amino]-4-methyl-5-thiazolecarboxylic acid Et ester (F1) and 2-[4,6-bis(4-hydroxypiperidin-1-yl)pyrimidin-2-ylamino]-4-methylthiazole-5-carboxylic acid Et ester (F2) are reported. F1 is 100 fold selective for PDE 7 over PDE 4 and F2 is >50 fold selective for PDE 7. The IC50 for lipolysaccharide peripheral blood mononuclear cells tumor necrosis factors (LPS PBMC TNF) was >25 μM for F2 while cilomilast was potent in this assay with an IC50 of 0.43 μM. Mice were administered 30 mg/kg IP of F1 and 45 min later were administered 10 mg of rolipram orally; the Cmax for F1 are essentially unchanged by co-administration of rolipram, and the Cmax of rolipram was reduced by a factor of 3 by co-administration with F1. Also, the plasma concentration of F1 when administered at 30 mg/kg does not reach the PDE 4 IC50 of F1. Compared to LPS-injected mice pretreated with vehicle, mice receiving F1 or rolipram alone had 52% and 54% redns. in serum TNF, resp. (each p<.05 vs. vehicle), as measured by a specific immunoassay, whereas mice treated with the combination of rolipram plus F1 showed an 89% reduction in serum TNF, which was significantly (p<.05) less than mice receiving either compound alone. Mice treated with dexamethasone showed a 93% reduction in serum TNF. Compound F2 inhibited TNF production by 33.7% which was not statistically significant, whereas cilomilast inhibited TNF production by 56% (p < 0.05); the combination group which received both cilomilast 1 mg/kg and compound F2, had a decrease in TNF production of 72% (p < 0.05 vs. cilomilast alone). Although the methods of preparation are not claimed, 27 example prepns. are included.

AN 2002:849588 HCAPLUS <<LOGINID::20090206>>

DN 137:353054

TI Preparation of pyrimidinylaminothiazolecarboxylates and related pyrimidines as dual inhibitors of phosphodiesterases PDE 7 and PDE 4

IN Pitts, William John; Watson, Andrew J.; Dodd, John H.

PA Bristol-Myers Squibb Company, USA

SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002088080	A2	20021107	WO 2002-US13742	20020430 <--
	WO 2002088080	A3	20030313		
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	AU 2002256419	A1	20021111	AU 2002-256419	20020430 <--
	US 20030104974	A1	20030605	US 2002-135998	20020430 <--
	EP 1383743	A2	20040128	EP 2002-725882	20020430 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	HU 2004000718	A2	20040728	HU 2004-718	20020430 <--

	JP 2004532233	T	20041021	JP 2002-585382	20020430 <--
	US 20060116516	A1	20060601	US 2005-281246	20051117 <--
PRAI	US 2001-287964P	P	20010501	<--	
	US 2001-299287P	P	20010619	<--	
	US 2002-368752P	P	20020329		
	WO 2002-US13742	W	20020430		
	US 2002-173322	A3	20020617		

OS MARPAT 137:353054

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 11 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Preparation of pyrimidinylaminothiazolecarboxylates and related pyrimidines as dual inhibitors of phosphodiesterases PDE 7 and PDE 4

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Dual inhibitors of PDE7 and PDE4, together with their use to treat leukocyte activation-associated disorders (including transplant rejection, rheumatoid arthritis, inflammatory bowel disease, psoriasis, asthma, chronic obstructive pulmonary disease, lupus and multiple sclerosis), are provided herein. Dual inhibitors of PDE 7 and PDE 4 (pyrimidines, e.g. I), together with their use to treat leukocyte activation-associated disorders (including transplant rejection, rheumatoid arthritis, inflammatory bowel disease, psoriasis, asthma, chronic obstructive pulmonary disease, lupus and multiple sclerosis), are provided herein. The present invention further provides for a method of reducing or alleviating nausea and emesis associated with the administration of PDE4 inhibitors comprising either the administration of a dual PDE 7-PDE 4 inhibitor, or the simultaneous or sequential co-administration of a selective PDE 7 inhibitor together with a selective PDE 4 inhibitor. In I, R1a is H or alkyl; R2a is optionally substituted heteroaryl; Z is halogen, alkyl, substituted alkyl, haloalkyl, or NR3aR4a; R3a is H or alkyl; R4a is alkyl, optionally substituted (heteroaryl)alkyl, optionally substituted heterocyclo, optionally substituted (heterocyclo)alkyl, or (aryl)alkyl wherein the aryl group is substituted with one or two groups T1* and T2* and optionally further substituted with a group T3*; or R3a and R4a together with the N atom to which they are attached may combine to form an optionally substituted heterocyclo ring; R5a is (aryl)alkyl wherein the aryl group is substituted with one or two groups T1* and T2* and optionally further substituted with a group T3*; R6a is H or alkyl; R7a is H or alkyl; T1* and T2* are independently alkoxy, alkoxycarbonyl, heteroaryl or -SO2R8a where R8a is alkyl, amino, alkylamino or dialkylamino; or T1* and T2* together with the atoms to which they are attached may combine to form a ring (e.g., benzodioxole); T3* is H, alkyl, halo, haloalkyl or cyano. Other pyrimidine classes (II-V) are described in the claims; this patent differs om WO 02/088080 with regard to IV (J1 and J2 are same or different and are a bond or optionally substituted alkylene group of 1-4 C atoms, provided that they are not both a bond, and further that if one is a bond the other is an alkylene group of at least 3 C atoms). Pharmaceutical properties for 2-[[4-[4-(dimethylamino)-1-piperidinyl]-6-[[(3,4,5-trimethoxyphenyl)methyl]amino]-2-pyrimidinyl]amino]-4-methyl-5-thiazolecarboxylic acid Et ester (F1) and 2-[4,6-bis(4-hydroxypiperidin-1-yl)pyrimidin-2-ylamino]-4-methylthiazole-5-

carboxylic acid Et ester (F2) are reported. F1 is 100 fold selective for PDE 7 over PDE 4 and F2 is >50 fold selective for PDE 7. The IC50 for lipolysaccharide peripheral blood mononuclear cells tumor necrosis factors (LPS PBMC TNF) was >25 μM for F2 while cilomilast was potent in this assay with an IC50 of 0.43 μM. Mice were administered 30 mg/kg IP of F1 and 45 min later were administered 10 mg of rolipram orally; the Cmax for F1 are essentially unchanged by co-administration of rolipram, and the Cmax of rolipram was reduced by a factor of 3 by co-administration with F1. Also, the plasma concentration of F1 when administered at 30 mg/kg does not reach the PDE 4 IC50 of F1. Compared to LPS-injected mice pretreated with vehicle, mice receiving F1 or rolipram alone had 52% and 54% redns. in serum TNF, resp. (each p<.05 vs. vehicle), as measured by a specific immunoassay, whereas mice treated with the combination of rolipram plus F1 showed an 89% reduction in serum TNF, which was significantly (p<.05) less than mice receiving either compound alone. Mice treated with dexamethasone showed a 93% reduction in serum TNF. Compound F2 inhibited TNF production by 33.7% which was not statistically significant, whereas cilomilast inhibited TNF production by 56% (p < 0.05); the combination group which received both cilomilast 1 mg/kg and compound F2, had a decrease in TNF production of 72% (p < 0.05 vs. cilomilast alone). Although the methods of preparation are not claimed, 27 example prepns. are included.

AN 2002:849587 HCAPLUS <<LOGINID::20090206>>

DN 137:353053

TI Preparation of pyrimidinylaminothiazolecarboxylates and related pyrimidines as dual inhibitors of phosphodiesterases PDE 7 and PDE 4

IN Pitts, William John; Watson, Andrew J.; Dodd, John H.

PA Bristol-Myers Squibb Company, USA

SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002088079	A2	20021107	WO 2002-US13628	20020429 <--
	WO 2002088079	A3	20030130		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002305290	A1	20021111	AU 2002-305290	20020429 <--
	US 20030104974	A1	20030605	US 2002-135998	20020430 <--
	US 20060116516	A1	20060601	US 2005-281246	20051117 <--
PRAI	US 2001-287964P	P	20010501	<--	
	US 2001-299287P	P	20010619	<--	
	US 2002-368752P	P	20020329		
	WO 2002-US13628	W	20020429		
	US 2002-173222	A3	20020617		

OS MARPAT 137:353053

L27 ANSWER 12 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Treatment of respiratory and lung diseases with antisense oligonucleotides and a bronchodilating agent

AB This patent relates to a composition comprising a carrier, oligonucleotides

(oligos) that are antisense to adenosine receptors, and contain low amts. of or no adenosine (A), plus bronchodilating agents. All antisense oligonucleotides designed in accordance with the invention were highly effective at countering or reducing effects mediated by the receptors to which they are targeted. Two antisense phosphorothioated oligos targeting human adenosine A1 receptor mRNA, one targeting adenosine A2b receptor, and two targeting an A3 receptor are capable of countering the effect of exogenously administered adenosine which is mediated by the specific receptor they are targeted to. The activity of the antisense oligos are specific to the target and substitutively fail to inhibit another target. An oligonucleotide wherein the phosphodiester bonds are substituted with phosphorothioate bonds evidenced an unexpected superiority over the phosphodiester antisense oligo. In addition, they result in extremely low or non-existent deleterious side effects or toxicity. This represents 100% success in providing agents that are highly effective and specific in the treatment of bronchoconstriction and/or inflammation. These agents and the composition and formulations provided are suitable for the treatment of respiratory tract, pulmonary and malignant diseases associated with bronchoconstriction, respiratory tract inflammation and allergies, impaired airways, including lung disease and diseases whose secondary effects afflict the lungs of a subject, such as allergies, asthma, impeded respiration, allergic rhinitis, pain, cystic fibrosis, pulmonary fibrosis, RDA, COPD, and cancers, among others. The present agents and composition may be administered preventatively, prophylactically or therapeutically in conjunction with other therapies, or may be utilized as a substitute for therapies that have significant, neg. side effects. The method of the present invention is also practiced with antisense oligonucleotides targeted to many genes, mRNAs and their corresponding proteins in essential the same manner.

AN 2002:832576 HCAPLUS <<LOGINID::20090206>>

DN 137:346197

TI Treatment of respiratory and lung diseases with antisense oligonucleotides and a bronchodilating agent

IN Nyce, Jonathan W.; Li, Yukui; Sandrasagra, Anthony; Katz, Evan; Pabalan, Jonathan; Aguilar, Douglas; Miller, Shoreh; Tang, Lei; Shahabuddin, Syed

PA Epigenesis Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 764 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002085309	A2	20021031	WO 2002-US13143	20020423 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
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	AU 2002305236	A1	20021105	AU 2002-305236	20020423 <--
	US 20040049022	A1	20040311	US 2003-627930	20030725
PRAI	US 2001-286036P	P	20010424	<--	
	WO 2002-US13135	A2	20020423		
	WO 2002-US13143	W	20020423		

OS MARPAT 137:346197

L27 ANSWER 13 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Treatment of respiratory and lung diseases with antisense oligonucleotides and a bronchodilating agent

AB This patent relates to a composition comprising a carrier, oligonucleotides (oligos) that are antisense to adenosine receptors, and contain low amts. of or no adenosine (A), plus bronchodilating agents. All antisense oligonucleotides designed in accordance with the invention were highly effective at countering or reducing effects mediated by the receptors to which they are targeted. Two antisense phosphorothioated oligos targeting human adenosine A1 receptor mRNA, one targeting adenosine A2b receptor, and two targeting an A3 receptor are capable of countering the effect of exogenously administered adenosine which is mediated by the specific receptor they are targeted to. The activity of the antisense oligos are specific to the target and substitutively fail to inhibit another target. An oligonucleotide wherein the phosphodiester bonds are substituted with phosphorothioate bonds evidenced an unexpected superiority over the phosphodiester antisense oligo. In addition, they result in extremely low or non-existent deleterious side effects or toxicity. This represents 100% success in providing agents that are highly effective and specific in the treatment of bronchoconstriction and/or inflammation. Treatment with antisense oligonucleotides in combination with anti-inflammatory steroid and/or ubiquinones is also provided. These agents and the composition and formulations provided are suitable for the treatment of respiratory tract, pulmonary and malignant diseases associated with bronchoconstriction, respiratory tract inflammation and allergies, impaired airways, including lung disease and diseases whose secondary effects afflict the lungs of a subject, such as allergies, asthma, impeded respiration, allergic rhinitis, pain, cystic fibrosis, pulmonary fibrosis, RDA, COPD, and cancers, among others. The present agents and composition may be administered preventatively, prophylactically or therapeutically in conjunction with other therapies, or may be utilized as a substitute for therapies that have significant, neg. side effects. The method of the present invention is also practiced with antisense oligonucleotides targeted to many genes, mRNAs and their corresponding proteins in essential the same manner.

AN 2002:832575 HCAPLUS <<LOGINID::20090206>>
DN 137:346196

TI Treatment of respiratory and lung diseases with antisense oligonucleotides and a bronchodilating agent

IN Nyce, Jonathan W.; Li, Yukui; Sandrasagra, Anthony; Katz, Evan; Pabalan, Jonathan; Aguilar, Douglas; Miller, Shoreh; Tang, Lei; Shahabuddin, Syed
PA Epigenesis Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 872 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002085308	A2	20021031	WO 2002-US13135	20020423 <--
WO 2002085308	A3	20021219		

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WO 2002085308	A2	20021031	WO 2002-XA13135	20020423 <--

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    WO 2002085308       A2    20021031    WO 2002-XB13135        20020423 <--
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PRAI US 2001-286137P    P     20010424  <--
    WO 2002-US13135     A     20020423
    WO 2002-US13143     A2    20020423
OS  MARPAT 137:346196

L27 ANSWER 14 OF 48  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI  Preparation of thiazolyl-, oxazolyl-, pyrrolyl-, and imidazolyl- acid
    amide derivatives as inhibitors of phosphodiesterase IV
    isozymes
GI
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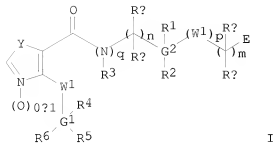
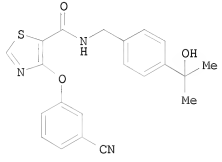


I



II

AB Title compds. I [wherein p = 0–1; q = 0–1; provided that when q = 0, n = 2; m = 0–3; n = 1–2; W1 and W2 = independently O, SO0–2, or NR3; or W2 = (un)substituted methylene; Y = SO0–2, O, NO0–1, NR3, or (un)substituted methylene; ; RA and RB = independently H, F, CF3, alkyl, or (un)substituted cycloalkyl, Ph, or benzyl; or when m = 1, CRARB = (un)substituted spiro; RC and RD have the same meaning as RA and RB except that one of them must be H; R1 and R2 = H, F, Cl, CN, NO2, (fluoro)alkyl, alkynyl, alkoxy, phenoxy, carbamoyl, etc.; R3 = H, alkyl, Ph, benzyl, alkoxy, phenoxy, etc.; R4, R5, and R6 = H, F, Cl, and (un)substituted (cyclo)alkyl, alkenyl, alkynyl, Ph, benzyl, pyridyl, alkoxy, phenoxy, acyl, carboxy, CN, NO2, carbamoyl, ureido, (hetero)aryl, etc.; G1 and G2 = independently (un)saturated carbocyclyl or heterocyclyl; E = (un)substituted carboxy, carbamoyl, acyl, hydroxyalkyl, cyanoalkyl, acylamino, ureido, amino, heterocyclyl, etc.] were prepared as inhibitors of PDE4 (no data). For example, 4-(3-cyanophenoxy)thiazole-5-carboxylic acid was treated with 2-(4-aminomethylphenyl)propan-2-ol in the presence of EDCl and HOBT in DMF to give the thiazolamide II. I are useful in the treatment of diseases regulated by the activation and degranulation of eosinophils, especially asthma, chronic bronchitis, and chronic obstructive pulmonary disease (no data). In addition, I may be used in combination therapy with a wide variety of other therapeutic agents.

AN 2002:594844 HCAPLUS <<LOGINID::20090206>>

DN 137:140518

TI Preparation of thiazolyl-, oxazolyl-, pyrrolyl-, and imidazolyl- acid amide derivatives as inhibitors of phosphodiesterase IV isozymes

IN Marfat, Anthony; McKechney, Michael William

PA Pfizer Products Inc., USA

SO PCT Int. Appl., 249 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2002060898	A1	20020808	WO 2001-IB2728	20011224	<--
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
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	AU 2002222429	A1	20020812	AU 2002-222429	20011224	<--
	EP 1355907	A1	20031029	EP 2001-273600	20011224	<--
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	BR 2001016850	A	20040225	BR 2001-16850	20011224	<--
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	US 20020123520	A1	20020905	US 2002-62145	20020131	<--
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	US 6894041	B2	20050517			
	US 20030186974	A1	20031002	US 2002-300950	20021120	<--
	US 6869945	B2	20050322			
	IN 2003MU00607	A	20050318	IN 2003-MU607	20030617	<--
	ZA 2003005769	A	20041025	ZA 2003-5769	20030725	<--
	BG 108039	A	20040730	BG 2003-108039	20030728	<--
	NO 2003003398	A	20030929	NO 2003-3398	20030730	<--
	MX 2003006886	A	20031113	MX 2003-6886	20030730	<--
PRAI	US 2001-265486P	P	20010131	<--		
	WO 2001-IB2728	W	20011224	<--		
	US 2002-62145	A3	20020131			

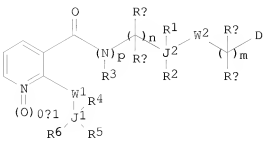
OS MARPAT 137:140518

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 15 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Preparation of carbamoyl-substituted pyridinyl aryl ether derivatives as inhibitors of phosphodiesterase IV isozymes

GI



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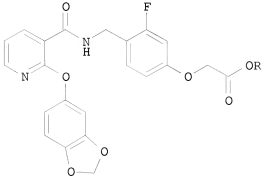

II

AB Title compds. compds. I [wherein p = 0-1, provided that when p = 0, n = 2; m = 1-3; n = 1-2; W1 and W2 = independently O, S(O)0-2, or NR3; Y = =C(R1a) or N(O)0-1; R1a = H, F, Cl, CN, NO2, (fluoro)alkyl, alkynyl, fluoroalkoxy, OR16, or (un)substituted carbamoyl; RA and RB = independently H, F, CF3, or (un)substituted (cyclo)alkyl, Ph, or benzyl; or CRARB = spiro moiety; RC and RD = the same as RA and RB except that one of them must be H; R1 and R2 = independently H, F, Cl, CN, NO2, (fluoro)alkyl, alkynyl, OR16, or (un)substituted carbamoyl; R3 = H, alkyl, Ph, benzyl, or OR16; R4, R5 and R6 = independently H, F. Cl, alkynyl, R16, OR16, SO0-2R16, COR16, CO2R16, OCOR16, CN, NO2, (un)substituted carbamoyl(oxy), ureido, carboximidoyl, aryl, heterocyclyl, etc.; or R5 and R6 taken together with the atoms to which they are attached = (hetero)cyclyl; J1 and J2 = independently (un)substituted, (un)saturated monocyclic or fused polycyclic ring; D = (un)substituted carboxy, carbamoyl, acyl, hydroxy(alkyl), cyano(alkyl), etc.; R16 = H or (un)substituted (cyclo)alkyl, alkenyl, Ph, benzyl, or pyridyl] were prepared as inhibitors of PDE4 (no data). For example, 2-(benzo[1,3]dioxol-5-yloxy)nicotinic acid was coupled with (4-aminomethyl-3-fluorophenoxy)acetic acid Me ester in the presence of 1-hydroxybenzotriazole•H2O and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide•HCl in DMF/CH2Cl2 to give the pyridinecarboxamide II (R = Me) in 38% yield. Saponification using aqueous LiOH in THF and MeOH afforded the desired acid II (R = OH) in 21% yield. I are useful in the treatment of diseases regulated by the activation and degranulation of eosinophils, especially asthma, chronic bronchitis, and chronic obstructive pulmonary disease (no data). In addition, I may be used in combination therapy with a wide variety of other therapeutic agents.

AN 2002:594842 HCAPLUS <<LOGINID::20090206>>

DN 137:154859

TI Preparation of carbamoyl-substituted pyridinyl aryl ether derivatives as inhibitors of phosphodiesterase IV isozymes

IN Chambers, Robert James; Magee, Thomas Victor; Marfat, Anthony
PA Pfizer Products Inc., USA
SO PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2002060896	A1	20020808	WO 2001-IB2726	20011224	<--
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PRAI	US 2001-265304P	P	20010131	<--		
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OS MARPAT 137:154859
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 16 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Preparation of nicotinamide biaryl derivatives as inhibitors of PDE4 isozymes
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; g = 0–1; j = 0–1; provided that when j = 0, n must be 2; k = 0–1; m = 0–2; n = 1–2; W1 = O, SOt (t = 0–2), NR3; W2 = OCR9R10, or absent; Y = CR1, NOk (k = 0–1); R9, R10 = H, F, CF3, etc.; or R9 and R10 are taken together, but only in the case where m = 1, to form a spiro moiety; R7, R8 have the same meaning as R9, R10 except that one of them must be H; R1, R2 = H, F, Cl, etc.; R3 = H, alkyl, Ph, etc.; R4–R6 = H, F, Cl, etc.; Q1 = Ph, benzodioxyl, etc.; Q2 = biaryl moiety], useful as inhibitors of PDE4 in the treatment of diseases regulated by the activation and degranulation of eosinophils, especially asthma, chronic bronchitis, and chronic obstructive pulmonary disease, were prepared E.g., a multi-step synthesis of the amide II, starting from Me 3-bromobenzoate and 4-formylbenzeneboronic acid, was given. Compds. I showed anti-inflammatory activity at 0.0001 μM to 20.0 μM in whole blood assay for LTE4.

AN 2002:594822 HCAPLUS <<LOGINID::20090206>>

DN 137:154857

TI Preparation of nicotinamide biaryl derivatives as inhibitors of PDE4 isozymes

IN Chambers, Robert James; Magee, Thomas Victor; Marfat, Anthony

PA Pfizer Products Inc., USA

SO PCT Int. Appl., 224 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

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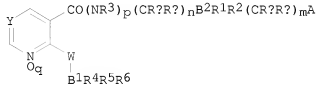
PRAI	US 2001-265492P	P	20010131	<--	
	WO 2001-IB2341	W	20011206	<--	
	US 2002-62813	A3	20020131		

OS MARPAT 137:154857
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 17 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Preparation of nicotinamides and mimetics as inhibitors of phosphodiesterase IV isozymes
GI



I

AB Title compds. [I; p, q = 0, 1; m = 0-2; n = 1, 2; A = CO2R7, CONR9CO2R7, CONR7R9, OP(O)(OH)2, SO3H, acylsulfonamido, etc.; W = O, S, SO, SO2, NR3; Y = N, NO, CR11; R1, R2 = H, F, Cl, cyano, NO2, alkyl, alkynyl, fluoroalkyl, etc.; R3 = H, alkyl, Ph, PhCH2, etc.; R4-R6 = H, F, Cl, alkynyl, cyano, NO2, etc.; R7 = H, (substituted) alkyl, alkenyl, alkynyl; R9 = H, alkyl, cycloalkyl, Ph, PhCH2, pyridyl, etc.; R11 = H, F, Cl, cyano, NO2, alkyl, alkynyl, fluoroalkyl, fluoroalkoxy, etc.; Ra, Rb = H, F, CF3, alkyl, (substituted) cycloalkyl, Ph, PhCH2; B1, B2 = 3-7 membered (hetero)cyclyl, 7-12 membered poly(hetero)cyclyl; pairs of variables may form rings; with provisos], were prepared (no data). Thus, Me 2-[4-[[[2-(benzo[1,3]dioxol-5-yloxy)pyridine-3-carbonyl]amino]methyl]phenyl]-2-methylpropionate was suspended in Me3COH. Aqueous NaOH was added to the suspension, and the reaction mixture was refluxed 1 h to give 2-[4-[[[2-(benzo[1,3]dioxol-5-yloxy)pyridine-3-carbonyl]amino]methyl]phenyl]-2-methylpropionic acid.
AN 2002:591707 HCAPLUS <<LOGINID::20090206>>
DN 137:140509
TI Preparation of nicotinamides and mimetics as inhibitors of phosphodiesterase IV isozymes
IN Chambers, Robert J.; Magee, Thomas V.; Marfat, Anthony
PA Pfizer Products Inc., USA
SO Eur. Pat. Appl., 180 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1229034	A1	20020807	EP 2002-250202	20020111 <--
	EP 1229034	B1	20050413		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	AT 293109	T	20050415	AT 2002-250202	20020111 <--
	ES 2239203	T3	20050916	ES 2002-250202	20020111 <--
	CA 2369462	A1	20020731	CA 2002-2369462	20020129 <--
	MX 2002001141	A	20020918	MX 2002-1141	20020130 <--
	US 20020111495	A1	20020815	US 2002-62811	20020131 <--
	JP 2002284766	A	20021003	JP 2002-22710	20020131 <--
	BR 2002000250	A	20021008	BR 2002-250	20020131 <--
	US 20040171798	A1	20040902	US 2004-781062	20040217 <--
	US 7250518	B2	20070731		

PRAI US 2001-265240P P 20010131 <--
US 1997-43403P P 19970404 <--
US 1998-105120P P 19981021 <--
US 2002-62811 B1 20020131
OS MARPAT 137:140509
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 18 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI The phosphodiesterase 4 inhibitor roflumilast is effective in the treatment of allergic rhinitis
AB The beneficial effects of phosphodiesterase 4 (PDE4) inhibitors in allergic asthma have been shown in previous preclin. and clin. studies. Because allergic rhinitis and asthma share several epidemiol. and pathophysiol. factors, PDE4 inhibitors might also be effective in allergic rhinitis. The main objective of this study was to investigate the efficacy of oral roflumilast (500 μg/day) in allergic rhinitis. In a randomized, placebo-controlled, double-blinded, crossover study, 25 subjects (16 male, 9 female; median age, 28 yr) with histories of allergic rhinitis but asymptomatic at screening received roflumilast (500 μg once daily) and placebo for 9 days each with a washout period of at least 14 days in between treatment periods. In each of the treatment periods, controlled intranasal allergen provocation with pollen exts. was performed daily beginning the third day of treatment, each time approx. 2 h after study drug administration. Five and 30 min after each allergen provocation, rhinal airflow was measured by means of anterior rhinomanometry and the subjective symptoms obstruction, itching, and rhinorrhea were assessed by means of a standardized visual analog scale. Rhinal airflow improved almost consistently during the 9 days of roflumilast treatment, and it was significantly higher at study day 9 on roflumilast in comparison with placebo, a result also found for itching and rhinorrhea. With respect to the subjective obstruction score, a significant difference in comparison with placebo could be demonstrated within 4 days. This study shows that a PDE4 inhibitor, roflumilast, effectively controls symptoms of allergic rhinitis. Thus PDE4 inhibitors might be a future treatment option not only in allergic asthma but also in allergic rhinitis or the combination of the 2 diseases.
AN 2001:810886 HCAPLUS <<LOGINID::20090206>>
DN 136:112393
TI The phosphodiesterase 4 inhibitor roflumilast is effective in the treatment of allergic rhinitis
AU Schmidt, Bernhard M. W.; Kusma, Matthias; Feuring, Martin; Timmer, Wolfgang E.; Neuhauser, Markus; Bethke, Thomas; Stuck, Boris A.; Hormann, Karl; Wehling, Martin
CS Institute of Clinical Pharmacology, Mannheim University Hospital, Ruprecht-Karls-University Heidelberg, Mannheim, D - 68167, Germany
SO Journal of Allergy and Clinical Immunology (2001), 108(4), 530-536
CODEN: JACIBY; ISSN: 0091-6749
PB Mosby, Inc.
DT Journal
LA English
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 19 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Theophylline Inhibits TNF-α-Induced CD4 Expression on Human Eosinophils and CD4+ Eosinophil Migration
AB Increasing evidence regarding asthma suggests that CD4+ cells are preferentially recruited to sites of bronchial inflammation.

Interleukin (IL)-16 has been reported as playing an important role in the accumulation of CD4+ cells. We have shown that the CD4 mol. is expressed on normal human eosinophils by tumor necrosis factor (TNF)-α stimulation. We evaluated the effects of theophylline, KF19514 [a selective phosphodiesterase (PDE) IV inhibitor] and dexamethasone on CD4 expression on eosinophils and eosinophil migration in response to IL-16, a natural soluble ligand of the CD4 mol. The maximum eosinophil migration was observed when eosinophils were cultured with TNF-α at 10 ng/mL for 18 h and the concentration of IL-16 was 10 pg/mL. CD4+ eosinophil migration in response to IL-16 was mostly, if not fully, chemokinetic and this migration was significantly inhibited by Fab of anti-CD4 monoclonal antibody. Theophylline (10-4-10-3 M), KF19514 (10-7-10-6 M) and dexamethasone (10-8-10-6 M) significantly inhibited CD4 expression on eosinophils induced by TNF-α. Theophylline (10-3 M) and KF19514 (10-6 M) inhibited CD4+ eosinophil migratory responses induced by IL-16, but 10-6 M dexamethasone did not. Theophylline and KF19514 augmented the intracellular adenosine-3',5'-cyclic monophosphate (cAMP) concentration in eosinophils, suggesting modulation by cAMP of CD4 expression and eosinophil migration. These data suggest that TNF-α-induced CD4+ eosinophils may contribute to eosinophil migratory responses induced by IL-16. Theophylline and selective PDE IV inhibitor may prevent airway inflammation by down-regulating CD4 expression on eosinophils and inhibiting eosinophil migration through CD4 and IL-16 interaction.

AN 2001:709567 HCAPLUS <<LOGINID::20090206>>
DN 137:27947
TI Theophylline Inhibits TNF-α-Induced CD4 Expression on Human Eosinophils and CD4+ Eosinophil Migration
AU Tsukadaira, Akihiro; Okubo, Yoshio; Horie, Shiro; Koyama, Sekiya
CS First Department of Internal Medicine, Shinshu University School of Medicine, Matsumoto, Japan
SO International Archives of Allergy and Immunology (2001), 125(4), 335-343
CODEN: IAAIEG; ISSN: 1018-2438
PB S. Karger AG
DT Journal
LA English
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 20 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Differential inhibition of equine neutrophil function by phosphodiesterase inhibitors
AB Neutrophils are recruited to the lungs of horses with chronic obstructive pulmonary disease (COPD) and exhibit increased activity after antigen challenge, which may contribute to inflammation and lung damage. Inhibition of phosphodiesterase isoenzymes (PDEs) has been shown to attenuate human neutrophil functions including superoxide production, leukotriene (LT)B4 biosynthesis, enzyme and chemokine release. As equine neutrophils contain predominantly the isoenzyme, PDE4, the present study was undertaken to investigate the effects of rolipram, a PDE4 inhibitor, on equine neutrophil function. For comparison, the effects of the nonselective PDE inhibitor, theophylline, were examined Cells from both normal horses and COPD horses in remission were used. Superoxide production was significantly inhibited by both rolipram [32.2±2.6 vs. 10.1±1.1 nmol/106 cells and 49.8±6.8 vs. 22.7±2.2 nmol/106 cells for normal and COPD susceptible horses, resp., in response to 10-7 M human recombinant (hr) C5a] and theophylline (19.0±0.6 vs. 10.2±0.6 nmol/106 cells and 24.3±2.1 vs. 10.7±0.9 nmol/106 cells for normal and COPD susceptible

horses, resp., in response to 10-7 M C5a). However, superoxide production induced by serum treated zymosan was inhibited only by theophylline (10-3 M). Neither hrC5a-nor platelet activating factor (PAF)-induced neutrophil adherence to fibronectin coated plastic was reduced by rolipram (10-5 M). These results demonstrate that the effects of PDE inhibitors on equine neutrophils are both stimulus and function dependent. The PDE4 inhibitors may reduce neutrophil activation in vivo in horses with COPD.

AN 2001:678448 HCAPLUS <<LOGINID::20090206>>
DN 136:363606
TI Differential inhibition of equine neutrophil function by phosphodiesterase inhibitors
AU Rickards, K. J.; Page, C. P.; Lees, P.; Cunningham, F. M.
CS Department of Veterinary Basic Sciences, The Royal Veterinary College, North Mymms, AL9 7TA, UK
SO Journal of Veterinary Pharmacology and Therapeutics (2001), 24(4), 275-281
CODEN: JVPTD9; ISSN: 0140-7783
PB Blackwell Science Ltd.
DT Journal
LA English
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 21 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Metalloproteinase inhibitors for the treatment of respiratory diseases
AB Use of a compound for the manufacture of a medicament for the treatment of a respiratory disease involving tissue destruction, wherein a compound has an inhibitory activity of greater than 50 inhibition of MMP1 or MMP2 or MMP8 or MMP9 at less than 100 μM concentration in an enzyme assay and which also downregulates in COPD lung tissue MMP1 or MMP2 or MMP8 or MMP9 to less than 50 of untreated levels at 100 μM.
AN 2001:635902 HCAPLUS <<LOGINID::20090206>>
DN 135:190419
TI Metalloproteinase inhibitors for the treatment of respiratory diseases
IN Richards, Andrew John McGlashan; Bannister, Robin Mark; Chaplin, Sharon Adele
PA Arakis Ltd., UK
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001062261	A1	20010830	WO 2001-GB814	20010226 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2399418	A1	20010830	CA 2001-2399418	20010226 <--
EP 1263443	A1	20021211	EP 2001-907907	20010226 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003523393	T	20030805	JP 2001-561326	20010226 <--
ZA 2002005357	A	20030818	ZA 2002-5357	20020704 <--

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     US 20030099600        A1    20030529    US 2002-227101         20020823 <--
PRAI GB 2000-4531          A     20000225  <--
     WO 2001-GB814         W     20010226  <--
RE.CNT  6      THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27  ANSWER 22 OF 48  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Phosphodiesterase inhibitors
AB   A review focuses on theophylline and inhibitors of type IV
     phosphodiesterase (PDE) and their roles in the treatment of asthma
     . The identification of many ways that cyclic nucleotide PDEs vary in
     their expression in different cells and tissues provides strong evidence
     that specific inhibitors could be developed in relation to different
     diseases.
AN   2001:562815  HCAPLUS <<LOGINID::20090206>>
DN   136:63429
TI   Phosphodiesterase inhibitors
AU   Cooper, Nicky; Krishna, Mamidipudi Thirumala; Gristwood, Robert; Holgate,
     Stephen
CS   Biology Celltech Chiroscience, Cambridge, UK
SO   Therapeutic Immunology (2nd Edition) (2001), 140-149.
     Editor(s): Austen, K. Frank. Publisher: Blackwell Science, Inc., Malden,
     Mass.
     CODEN: 69BPIR
DT   Conference; General Review
LA   English
RE.CNT  84     THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27  ANSWER 23 OF 48  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Involvement of A3 receptors in the potentiation by adenosine of the
     inhibitory effect of theophylline on human eosinophil degranulation:
     possible novel mechanism of the anti-inflammatory action of
     theophylline
AB   The current use of theophylline in asthma is based on both the
     bronchodilatory and the anti-inflammatory effects.  The exact
     mechanism of these actions is still controversial and may include the
     inhibition of adenosine 3',5'-monophosphate phosphodiesterase enzyme (PDE)
     and antagonism of adenosine receptors.  In this study, the mechanism of
     the anti-inflammatory action was investigated by studying the
     inhibition by theophylline of complement C5a-induced degranulation of
     human eosinophils and its interaction with adenosine.  Theophylline
     (10-1000 μM) inhibited C5a-induced release of eosinophil peroxidase
     (EPO) in a concentration-dependent manner with an ic50 of 233.5 μM and a
     maximal inhibition of 90.3 ± 3.0%.  In contrast, the PDE4
     inhibitor rolipram (up to 50 μM) had no effect.  The adenosine A3
     receptor agonist N6-(3-iodobenzyl)-5'-N-methylcarbamoyladenosine (IB-MECA)
     also inhibited release (ic50 = 7.5 μM), but neither adenosine itself
     nor the selective A1 and A2 agonists and antagonists had any significant
     effect, even at 100 μM.  The inhibition produced by clin. relevant
     concentration of theophylline (50 μM) was potentiated by ineffective concns.
     of exogenous adenosine and additive to that produced by IB-MECA.  The
     potent and selective A3 antagonist MRS 1220, but not the A1 or A2
     antagonists, significantly reversed the inhibitory effect of theophylline.
     These results suggest that therapeutic concns. of theophylline inhibit
     human eosinophil partly by acting as an A3 agonist.  Together with the
     potentiation of theophylline action by adenosine, perhaps via the A3
     receptors, these novel actions may, at least in part, contribute to the
     mechanism of the anti-inflammatory action of this drug in vivo.
AN   2001:373836  HCAPLUS <<LOGINID::20090206>>
DN   135:236094
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TI Involvement of A3 receptors in the potentiation by adenosine of the inhibitory effect of theophylline on human eosinophil degranulation: possible novel mechanism of the anti-inflammatory action of theophylline
AU Ezeamuzie, C. I.
CS Faculty of Medicine, Department of Pharmacology and Toxicology, Kuwait University, Safat, 13110, Kuwait
SO Biochemical Pharmacology (2001), 61(12), 1551-1559
CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier Science Inc.
DT Journal
LA English
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 24 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI In vivo efficacy in airway disease models of roflumilast, a novel orally active PDE4 inhibitor
AB We have investigated the bronchodilator and anti-inflammatory properties of roflumilast (3-cyclopropylmethoxy-4-difluoromethoxy-N-[3,5-dichloropyrid-4-yl]-b enzamide), a novel, highly potent, and selective phosphodiesterase 4 (PDE4) inhibitor. Addnl., we compared the effects of roflumilast and its N-oxide, the primary metabolite in vivo, with those of the PDE4 inhibitors piclamilast, rolipram, and cilomilast. Roflumilast inhibited the ovalbumin-evoked contractions of tracheal chains prepared from sensitized guinea pigs (EC50 = 2+10-7 M) but showed no relaxant effect on tissues contracted spontaneously. In spasmogen-challenged rats and guinea pigs, i.v. administered roflumilast displayed bronchodilatory activity (ED50 = 4.4 and 7.1 μmol/kg, resp.). Furthermore, roflumilast dose dependently attenuated allergen-induced bronchoconstriction in guinea pigs (ED50 = 0.1 μmol/kg i.v.). Roflumilast given orally (ED50 = 1.5 μmol/kg) showed equal potency to its N-oxide (ED50 = 1.0 μmol/kg) but was superior to piclamilast (ED50 = 8.3 μmol/kg), rolipram (ED50 = 32.5 μmol/kg), and cilomilast (ED50 = 52.2 μmol/kg) in suppressing allergen-induced early airway reactions. To assess the anti-inflammatory potential of orally administered roflumilast, antigen-induced cell infiltration, total protein, and TNFα concentration in bronchoalveolar lavage fluid of Brown Norway rats were determined Roflumilast and its N-oxide equally inhibited eosinophilia (ED50 = 2.7 and 2.5 μmol/kg, resp.), whereas the reference inhibitors displayed lower potency (ED50 = 17-106 μmol/kg). Besides, orally administered roflumilast abrogated LPS-induced circulating TNFα in the rat (ED50 = 0.3 μmol/kg), an effect shared by its N-oxide, with both mols. exhibiting 8-, 25-, and 310-fold superiority to piclamilast, rolipram, and cilomilast, resp. These results, coupled with the in vitro effects of roflumilast on inflammatory cells, suggest that roflumilast represents a potential new drug for the treatment of asthma and chronic obstructive pulmonary disease.
AN 2001:240840 HCAPLUS <<LOGINID::20090206>>
DN 135:86928
TI In vivo efficacy in airway disease models of roflumilast, a novel orally active PDE4 inhibitor
AU Bundschuh, Daniela S.; Eltze, Manfrid; Barsig, Johannes; Wollin, Lutz; Hatzelmann, Armin; Beume, Rolf
CS Department of Pharmacology, Byk Gulden, Konstanz, Germany
SO Journal of Pharmacology and Experimental Therapeutics (2001), 297(1), 280-290
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal

LA English
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 25 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Anti-inflammatory and immunomodulatory potential of the novel PDE4 inhibitor roflumilast in vitro
AB From a series of benzamide derivs., roflumilast (3-cyclopropylmethoxy-4-difluoromethoxy-N-[3,5-di-chloropyrid-4-yl]b enzamide) was identified as a potent and selective PDE4 inhibitor. It inhibits PDE4 activity from human neutrophils with an IC50 of 0.8 nM without affecting PDE1 (bovine brain), PDE2 (rat heart), and PDE3 and PDE5 (human platelets) even at 10,000-fold higher concns. Roflumilast is almost equipotent to its major metabolite formed in vivo (roflumilast N-oxide) and piclamilast (RP 73401), however, more than 100-fold more potent than rolipram and Ariflo (cilomilast; SB 207499). The anti-inflammatory and immunomodulatory potential of roflumilast and the reference compds. was investigated in various human leukocytes using cell-specific responses: neutrophils [N-formyl-methyl-leucyl-phenylalanine (fMLP)-induced formation of LTB4 and reactive oxygen species (ROS)], eosinophils (fMLP- and C5a-induced ROS formation), monocytes, monocyte-derived macrophages, and dendritic cells (lipopolysaccharide-induced tumor necrosis factor-α synthesis), and CD4+ T cells (anti-CD3/anti-CD28 monoclonal antibody-stimulated proliferation, IL-2, IL-4, IL-5, and interferon-γ release). Independent of the cell type and the response investigated, the corresponding IC values (for half-maximum inhibition) of roflumilast were within a narrow range (2-21 nM), very similar to roflumilast N-oxide (3-40 nM) and piclamilast (2-13 nM). In contrast, cilomilast (40-3000 nM) and rolipram (10-600 nM) showed greater differences with the highest potency for neutrophils. Compared with neutrophils and eosinophils, representing the terminal inflammatory effector cells, the relative potency of roflumilast and its N-oxide for monocytes, CD4+ T cells, and dendritic cells is substantially higher compared with cilomilast and rolipram, probably reflecting an improved immunomodulatory potential. The efficacy or roflumilast in vitro and in vivo (see accompanying article in this issue) suggests that roflumilast will be useful in the treatment of chronic inflammatory disorders such as asthma and chronic obstructive pulmonary disease.
AN 2001:240839 HCAPLUS <<LOGINID::20090206>>
DN 135:28819
TI Anti-inflammatory and immunomodulatory potential of the novel PDE4 inhibitor roflumilast in vitro
AU Hatzelmann, Armin; Schudt, Christian
CS Department of Biochemistry, Byk Gulden, Konstanz, Germany
SO Journal of Pharmacology and Experimental Therapeutics (2001), 297(1), 267-279
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 26 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Antiasthmatic effect of YM976, a novel PDE4 inhibitor, in guinea pigs
AB YM976 is a novel and specific phosphodiesterase 4 inhibitor. In the authors' previous report, the authors indicated that YM976 has less emetogenicity, a major adverse effect of PDE4 inhibitors, than rolipram. In the present study, the authors examined the

antiasthmatic effects of YM976 in guinea pigs. YM976 orally administered exhibited inhibition of antigen-induced bronchoconstriction, airway plasma leakage, airway eosinophil infiltration, and airway hyperreactivity (AHR), with ED50 values of 7.3, 5.7, 1.0, and 0.52 mg/kg, resp. Rolipram also dose dependently suppressed these responses. Prednisolone suppressed eosinophil infiltration and AHR, whereas it failed to inhibit bronchoconstriction and plasma leakage. Theophylline moderately suppressed bronchoconstriction and edema, but neither eosinophil infiltration nor AHR. YM976 suppressed the peroxidase activity in the bronchoalveolar lavage fluid, and elevated the intracellular peroxidase activity and cAMP contents of infiltrated cells, suggesting that YM976 inhibited not only the infiltration but also the activation of leukocytes. In vitro studies revealed that YM976 potently suppressed eosinophil activation (EC30 = 83 nM), and exerted a little relaxation on LTD4-precontracted tracheal smooth muscle (EC50 = 370 nM). Rolipram exhibited a potent tracheal relaxation activity (EC50 = 50 nM). In vivo studies indicated that the inhibitory effect of YM976 on LTD4-induced bronchospasm was marginal even at 30 mg/kg p.o., although rolipram significantly inhibited the bronchospasm at the same dose. These results suggested that YM976, unlike rolipram, showed the inhibition of antigen-induced airway responses due to anti-inflammatory effects, but not to direct tracheal relaxation. In conclusion, YM976 may have potential therapeutic value in the treatment of asthma through its anti-inflammatory activities.

AN 2001:240826 HCAPLUS <<LOGINID::20090206>>
DN 135:28818
TI Antiasthmatic effect of YM976, a novel PDE4 inhibitor, in guinea pigs
AU Aoki, Motonori; Yamamoto, Satoshi; Kobayashi, Miki; Ohga, Keiko; Kanoh, Hiroyuki; Miyata, Keiji; Honda, Kazuo; Yamada, Toshimitsu
CS Inflammation Research Pharmacology Laboratories, Institute for Drug Discovery Research, Yamanouchi Pharmaceutical Co., Ltd., Tsukuba, Japan
SO Journal of Pharmacology and Experimental Therapeutics (2001), 297(1), 165-173
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 27 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Roflumilast: antiallergy/antiasthmatic, treatment of COPD, phosphodiesterase 4 inhibitor
AB A review with 16 refs. regarding the drug roflumilast which is used to treat chronic obstructive pulmonary disease (COPD) and asthma. Topics discussed include its synthesis, description, pharmacol. actions, and clin. studies.
AN 2001:196352 HCAPLUS <<LOGINID::20090206>>
DN 135:161992
TI Roflumilast: antiallergy/antiasthmatic, treatment of COPD, phosphodiesterase 4 inhibitor
AU Sorbera, L. A.; Leeson, P. A.; Castaner, J.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (2000), 25(12), 1261-1264
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 28 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Treatment of obstructive airways diseases with compositions comprising propylsulfonylethylaminoethyl benzothiazolone and PDE4 inhibitors
AB The present invention provides a pharmaceutical composition, pharmaceutical product or kit comprising a first active ingredient (A) being 4-hydroxy-7-[2-[2-[3-[2-phenylethoxy]propylsulfonyl]ethylamino]ethyl]-1,3-benzothiazol-2(3H)-one (I) or a pharmaceutically acceptable salt thereof, and a second active ingredient (B) being a PDE4 inhibitor, for use in the treatment of obstructive airways diseases. Antiinflammatory efficacy of a combination of 10 mg/kg oral ariflo and 0.3 g/kg aerosol I was shown in rats.
AN 2001:136925 HCAPLUS <<LOGINID::20090206>>
DN 134:188213
TI Treatment of obstructive airways diseases with compositions comprising propylsulfonylethylaminoethyl benzothiazolone and PDE4 inhibitors
IN Ince, Francis; Dixon, John; Holt, Philip
PA AstraZeneca UK Limited, UK
SO PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001011933	A2	20010222	WO 2000-GB3114	20000814 <--
	WO 2001011933	A3	20010614		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2000064602	A	20010313	AU 2000-64602	20000814 <--
PRAI	SE 1999-2937	A	19990818	<--	
	WO 2000-GB3114	W	20000814	<--	

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 29 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Synergistic combination comprising roflumilast and a PDE-3 inhibitor
AB The invention relates to the combined use of the PDE4 inhibitor roflumilast, its salts or its N-oxide with a PDE3 inhibitor for the treatment of certain disease conditions such as acute or chronic obstructions of the bronchi. The dose in the case of PDE-3 inhibitor is typically in the range 0.1-25 mg/kg/day and the drugs can be administered as tablets, capsules, solns., etc.
AN 2000:790311 HCAPLUS <<LOGINID::20090206>>
DN 133:340267
TI Synergistic combination comprising roflumilast and a PDE-3 inhibitor
IN Amschler, Hermann; Beume, Rolf; Hafner, Dietrich; Schudt, Christian; Hatzelmann, Armin; Kilian, Ulrich
PA Byk Gulden Lomberg Chemische Fabrik Gmbh, Germany
SO PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000066123	A1	20001109	WO 2000-EP3838	20000427 <--
	W: AE, AL, AU, BA, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2372850	A1	20001109	CA 2000-2372850	20000427 <--
	EP 1176960	A1	20020206	EP 2000-927094	20000427 <--
	EP 1176960	B1	20040929		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002543133	T	20021217	JP 2000-615008	20000427 <--
	AT 277616	T	20041015	AT 2000-927094	20000427 <--
	PT 1176960	T	20050228	PT 2000-927094	20000427 <--
	ES 2228512	T3	20050416	ES 2000-927094	20000427 <--
	US 6498173	B1	20021224	US 2001-959599	20011213 <--
	US 20030050329	A1	20030313	US 2002-286915	20021104 <--
	US 6897229	B2	20050524		
PRAI	EP 1999-108808	A	19990504 <--		
	WO 2000-EP3838	W	20000427 <--		
	US 2001-959599	A3	20011213 <--		

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 30 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Low adenosine anti-sense oligonucleotide, compositions, kit and method for treatment of airway disorders associated with bronchoconstriction, lung inflammation, allergy(ies) and surfactant depletion

AB An in vivo method of selectively delivering a nucleic acid to a target gene or mRNA, comprises the topical administration, e.g. to the respiratory system, of a subject of a therapeutic amount of an oligonucleotide (oligo) that is antisense to the initiation codon region, the coding region, the 5' or 3' intron-exon junctions or regions within 2 to 10 nucleotides of the junctions of the gene or antisense to a mRNA complementary to the gene in an amount effective to reach the target polynucleotide and reducing or inhibiting expression. In addition a method of treating an adenosine-mediated effect comprises topically administering to a subject an antisense oligo in an amount effective to treat the respiratory, pulmonary, or airway disease. In order to minimize triggering adenosine receptors by their metabolism, the administered oligos have a low content of or are essentially free of adenosine. A pharmaceutical composition and formulations comprise the oligo antisense to an adenosine receptor, genes and mRNAs encoding them, genomic and mRNA flanking regions, intron and exon borders and all regulatory and functionally related segments of the genes and mRNAs encoding the polypeptides, their salts and mixts. Various formulations contain a requisite carrier, and optionally other additives and biol. active agents. The low-adenosine or adenosine-free (des-A) agent for practicing the method of the invention may be prepared by selecting a target gene(s), genomic flanking region(s), RNA(s) and/or polypeptide(s) associated with a disease(s) or condition(s) afflicting lung airways, obtaining the sequence of the mRNA(s) corresponding to the target gene(s) and/or genomic flanking region(s), and/or RNAs encoding the target polypeptide(s), selecting at least one segment of the mRNA which may be up to 60 % free of thymidine (T) and synthesizing one or more anti-sense oligonucleotide(s) to the mRNA segments which are free of adenosine (A) by substituting a universal base for A when present in the oligonucleotide. The agent may be prepared by selection of target nucleic acid sequences with GC running stretches,

which have low T content, and by optionally replacing A in the antisense oligonucleotides with a "Universal or alternative base". The agent, composition and formulations are used for prophylactic, preventive and therapeutic treatment of ailments associated with impaired respiration, lung allergy(ies) and/or inflammation and depletion lung surfactant or surfactant hypoprodn., such as pulmonary vasoconstriction, inflammation, allergies, allergic rhinitis, asthma, impeded respiration, lung pain, cystic fibrosis, bronchoconstriction. The present treatment is suitable for administration in combination with other treatments, e.g. before, during and after other treatments, including radiation, chemotherapy, antibody therapy and surgery, among others. Alternatively, the present agent is effectively administered prophylactically or therapeutically by itself for conditions without known therapies or as a substitute for therapies exhibiting undesirable side effects. The treatment of this invention may be administered directly into the respiratory system of a subject so that the agent has direct access to the lungs, or by other effective routes of administration, e.g. topically, transdermally, by implantation, etc., in an amount effective to reduce or inhibit the symptoms of the ailment.

AN 2000:756484 HCAPLUS <<LOGINID::20090206>>

DN 133:329593

TI Low adenosine anti-sense oligonucleotide, compositions, kit and method for treatment of airway disorders associated with bronchoconstriction, lung inflammation, allergy(ies) and surfactant depletion

IN Nyce, Jonathan W.

PA East Carolina University, USA

SO PCT Int. Appl., 1592 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000062736	A2	20001026	WO 2000-US8020	20000324 <--
	WO 2000062736	A3	20011011		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2330022	A1	20001026	CA 2000-2330022	20000324 <--
	BR 2000006019	A	20010313	BR 2000-6019	20000324 <--
	EP 1168919	A2	20020109	EP 2000-919668	20000324 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003515525	T	20030507	JP 2000-611873	20000324 <--
	MX 2000012093	A	20010521	MX 2000-12093	20001206 <--
	AU 2002050710	A	20020808	AU 2002-50710	20020628 <--
PRAI	US 1999-127958P	P	19990406	<--	
	WO 2000-US8020	W	20000324	<--	
	AU 2000-71749	A3	20001122	<--	

OS MARPAT 133:329593

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 31 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN

TI The mechanism of apoptosis induced by theophylline in IL-5-activated eosinophils

AB Eosinophils play a key role in allergic inflammation and their survival is prolonged by IL-5 and GM-CSF in allergic patients. We previously reported that theophylline inhibited the IL-5-dependent prolongation of eosinophils by inducing apoptosis in vitro. This study deals with its mechanisms. The apoptosis was analyzed by means of PI staining. Western blot was applied to detect apoptosis-related proteins. Theophylline, a PDE IV inhibitor rolipram, PDE III inhibitors amrinone and cilostazol, as well as di-Bu cAMP induced eosinophil apoptosis. These agents increased intracellular cAMP, and activated caspase 8 and caspase 3 which play important roles in signal transduction and the execution of apoptosis. In conclusion, theophylline induced apoptosis in eosinophils through an increase in cAMP and activation of caspases.

AN 2000:506068 HCAPLUS <<LOGINID::20090206>>

DN 133:305404

TI The mechanism of apoptosis induced by theophylline in IL-5-activated eosinophils

AU Murata, Machiko

CS Department of Medicine, Teikyo University School of Medicine, Japan

SO Teikyo Igaku Zasshi (2000), 23(1), 27-38
CODEN: TIGZDZ; ISSN: 0387-5547

PB Teikyo Daigaku Igakubu

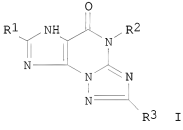
DT Journal

LA Japanese

L27 ANSWER 32 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors

GI



I

AB Tricyclic N heterocycles I [R1 = C1-5 alkyl, C5-6 cycloalkyl, Ph, PhCH2, 5- or 6-membered heterocyclic ring; R2 = C1-5 alkyl, C2-4 alkenyl; R3 = (substituted) C1-5 alkyl, (substituted) C5-6 cycloalkyl] and their salts are phosphodiesterase IV inhibitors and are potentially useful as vasodilators, inflammation inhibitors, and antiallergic agents. Thus, I (R1 = cyclopentyl, R2 = n-Pr, R3 = i-Pr) inhibited human monocyte phosphodiesterase IV with an IC50 of 0.018 μm. A tablet formulation contained I 80, corn starch 190, lactose 55, microcryst. cellulose 35, PVP 15, Na carboxymethylstarch 23, and Mg stearate 2 mg.

AN 2000:420941 HCAPLUS <<LOGINID::20090206>>

DN 133:53696

TI Tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors

IN Hoffmann, Matthias; Jung, Birgit; Kuefner-Muehl, Ulrike; Meade, Christopher John Montague

PA Boehringer Ingelheim Pharma K.-G., Germany

SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000035428	A2	20000622	WO 1999-EP9086	19991124 <--
	WO 2000035428	A3	20000928		
	W: CA, JP, MX, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	DE 19858331	A1	20000621	DE 1998-19858331	19981217 <--
	CA 2345752	A1	20000622	CA 1999-2345752	19991124 <--
	EP 1140098	A2	20011010	EP 1999-959324	19991124 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6417190	B1	20020709	US 1999-458789	19991210 <--
	MX 2001005936	A	20011203	MX 2001-5936	20010612 <--
PRAI	DE 1998-19858331	A	19981217	<--	
	US 1999-127777P	P	19990405	<--	
	WO 1999-EP9086	W	19991124	<--	

OS MARPAT 133:53696
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 33 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Phosphodiesterase 4 inhibitors and the treatment of asthma: where are we now and where do we go from here?
AB A review with 220 refs. Research conducted over the last 20 yr has established that inflammation of the airways is central to the airway dysfunction that characterizes asthma. Typically, the airway wall is infiltrated by a variety of cells including mast cells, eosinophils and T lymphocytes, which have deviated towards a TH2 phenotype. Together, these cells release a plethora of mediators including interleukin (IL)-4, IL-5, granulocyte/macrophage colony-stimulating factor and eotaxin which ultimately cause the histopathol. and symptoms of asthma. Glucocorticosteroids are the only drugs currently available that effectively impact upon this inflammation and resolve, to a greater or lesser extent, compromised lung function. However, steroids are nonselective and generally unsuitable for pediatric use. New drugs are clearly required. One group of potential therapeutic agents for asthma are inhibitors of cAMP-specific phosphodiesterase (PDE), of which theophylline may be considered a prototype. It is now known that PDE is a generic term which refers to at least 11 distinct enzyme families that hydrolyze cAMP and/or cGMP. Over the last decade, inhibitors of PDE4 (a cAMP-specific family that neg. regulates the function of almost all pro-inflammatory and immune cells, and exerts widespread anti-inflammatory activity in animal models of asthma) have been developed with the view to reducing the adverse effects profile associated with non-selective inhibitors such as theophylline. Such is the optimism regarding PDE4 as a viable therapeutic target that more than 100 PDE4 inhibitor patent applications have been filed since 1996 by 13 major pharmaceutical companies. This article reviews the progress of PDE4 inhibitors as anti-inflammatory agents, and identifies problems that have been encountered by the pharmaceutical industry in the clin. development of these drugs and what strategies are being considered to overcome them.
AN 2000:220582 HCAPLUS <<LOGINID::20090206>>
DN 132:231378

TI Phosphodiesterase 4 inhibitors and the treatment of asthma: where are we now and where do we go from here?
AU Giembycz, Mark A.
CS Thoracic Medicine, Imperial College of School of Medicine at the National Heart and Lung Institute, London, UK
SO Drugs (2000), 59(2), 193-212
CODEN: DRUGAY; ISSN: 0012-6667
PB Adis International Ltd.
DT Journal; General Review
LA English
RE.CNT 220 THERE ARE 220 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 34 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Phosphodiesterase and cyclic adenosine monophosphate-dependent inhibition of T-lymphocyte chemotaxis
AB There is abundant evidence for T-lymphocyte recruitment into the airways in allergic inflammatory responses. This study has tested the hypothesis that T-cell chemotaxis induced by platelet-activating factor (PAF) and human recombinant interleukin-8 (hr IL-8) can be attenuated by inhibition of phosphodiesterase activity and raised intracellular 3',5'-cyclic adenosine monophosphate (cAMP) levels. This study used theophylline, a nonselective phosphodiesterase (PDE) inhibitor, and rolipram, a selective PDE4 inhibitor, to study the effect of PDE inhibition on T-cell chemotaxis. The β2-adrenoceptor agonist, salbutamol, the adenylyl cyclase activator, forskolin, and the cAMP analog, dibutyryl cAMP (db-cAMP), were used to demonstrate a role for raised cAMP levels. T-cells were obtained from 10 atopic asthmatics, and the phenotype of migrating cells was examined by flow cytometry. Theophylline caused an inhibition of both PAF-and hrIL-8-induced chemotaxis (mean maximum inhibition at 1 mM: 73% and 48% for hrIL-8 and PAF, resp.) that was not specific for the CD4+, CD8+, CD45RO+, or CD45RA+ T-cell subsets. T-cell chemotaxis was more sensitive to treatment with rolipram whose effect was already significant from 0.1 μM on hrIL-8-induced chemotaxis. Both a low concentration of salbutamol (0.1 mM) and forskolin (10 μM) potentiated the inhibitory effect of a low concentration of theophylline (25 μM) on responses to PAF but not to hrIL-8. Finally, T-cell chemotaxis was also inhibited by db-cAMP. It is concluded that attenuation of T-cell chemotaxis to 2 chemoattractants of relevance to asthma pathogenesis can be achieved via phosphodiesterase inhibition and increased intracellular 3', 5'-cyclic monophosphate using drugs active on cyclic nucleotide phosphodiesterase. This action may explain the anti-inflammatory effects of theophylline and related drugs in asthma.
AN 2000:159549 HCAPLUS <<LOGINID::20090206>>
DN 132:288475
TI Phosphodiesterase and cyclic adenosine monophosphate-dependent inhibition of T-lymphocyte chemotaxis
AU Hidi, R.; Timmermans, S.; Liu, E.; Schudt, C.; Dent, G.; Holgate, S. T.; Djukanovic, R.
CS Southampton General Hospital, University Medicine, Southampton, SO16 6YD, UK
SO European Respiratory Journal (2000), 15(2), 342-349
CODEN: ERJOEI; ISSN: 0903-1936
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 35 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Inhibition of tracheal smooth muscle cell proliferation by phosphodiesterase inhibitors

AB Agents that increase intracellular cyclic 3',5'-adenosine monophosphate (cAMP), such as forskolin, prostaglandin (PG)E2, salbutamol and 8-bromo-cAMP, have been shown to inhibit the proliferation of airway smooth-muscle (ASM) cells in vitro. However, it has not yet been determined whether selective inhibitors of phosphodiesterase (PDE) isoenzymes III and IV that catalyze cAMP to 5'-adenosine monophosphate have the ability to inhibit ASM cell proliferation. To evaluate the effects of PDE inhibitors on ASM cell proliferation, ASM cells isolated from bovine tracheae were cultured in the presence of fetal bovine serum (FBS), with or without a non-selective PDE inhibitor (theophylline), a selective PDE III inhibitor (cilostazol), and a selective PDE IV inhibitor (rolipram). The number of ASM cells cultured with 5% FBS was significantly reduced by the presence of theophylline at 10-3 and 3 + 10-4 M, cilostazol at 10-5, 10-6 and 10-7 M, and rolipram at 10-4 and 10-5 M. The release of lactic dehydrogenase from ASM cells cultured with any concentration of these agents was not significantly different from that with medium alone. Inhibitors of PDE III and IV were demonstrated to have an inhibitory effect on ASM cell proliferation induced by FBS. The authors' results suggest the value of the further development of PDE inhibitors for the treatment of hyperplasia of ASM cells characteristic of airway remodeling, in addition to bronchospasm and airway inflammation, in bronchial asthma.

AN 2000:56603 HCAPLUS <<LOGINID::20090206>>

DN 132:303269

TI Inhibition of tracheal smooth muscle cell proliferation by phosphodiesterase inhibitors

AU Masu, Kazuko; Ohno, Isao; Yamaya, Mutsuo; Kawamura, Takeshi; Sasaki, Hidetada; Shirato, Kunio

CS First Department of Internal Medicine, Tohoku University School of Medicine, Sendai, 980-8574, Japan

SO Allergology International (1999), 48(4), 259-264
CODEN: ALINFR; ISSN: 1323-8930

PB Blackwell Science Asia Pty Ltd.

DT Journal

LA English

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 36 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Selective phosphodiesterase inhibitors for the treatment of bronchial asthma and chronic obstructive pulmonary disease

AB A review with 109 refs. Theophylline is commonly used in the treatment of obstructive airway diseases. The identification and functional characterization of different phosphodiesterase (PDE) isoenzymes has led to the development of various isoenzyme-selective inhibitors as potential anti-asthma drugs. Considering the distribution of isoenzymes in target tissues, with high activity of PDE3 and PDE4 in airway smooth muscle and inflammatory cells, selective inhibitors of these isoenzymes may add to the therapy of chronic airflow obstruction. However, initial data from clin. trials with selective PDE3 and PDE4 inhibitors have been somewhat disappointing and have tempered the expectations considerably since these drugs had limited efficacy and their use was clin. limited through side effects. The improved understanding of the mol. biol. of PDEs enabled the synthesis of novel drugs with an improved risk/benefit ratio. These "second generation" selective drugs have produced more promising clin. results not only for the treatment of bronchial asthma but also for the treatment of chronic obstructive pulmonary disease.

AN 1999:507374 HCAPLUS <<LOGINID::20090206>>
DN 131:153281
TI Selective phosphodiesterase inhibitors for the treatment of bronchial asthma and chronic obstructive pulmonary disease
AU Schmidt, D.; Dent, G.; Rabe, K. F.
CS Department of Pulmonology, Leiden University Medical Centre, Leiden, Neth.
SO Clinical and Experimental Allergy (1999), 29(Suppl. 2), 99-109
CODEN: CLEAEN; ISSN: 0954-7894
PB Blackwell Science Ltd.
DT Journal; General Review
LA English
RE.CNT 109 THERE ARE 109 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 37 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Antisense oligonucleotides capable of binding to multiple targets and their use in the treatment of respiratory disease
AB Antisense oligonucleotides carrying sequences that will allow them to bind to more than one mRNA in a target cell are described. Such oligonucleotides can be used as a single treatment for diseases having more than one contributing pathway. In particular, oligonucleotides effective against genes involved in the etiol. of respiratory disease are targeted. Preferably, the oligonucleotides are low in adenosine (≤15%) and may have adenosines substituted with analogs. These oligonucleotides are targeted to high (G+C) sequences within mRNAs. Thus, phosphorothioate antisense oligonucleotide (HAdA1AS, 5'-gatggagggcggcatggcggg-3') designed for the adenosine A1 receptor is provided. HAdA1AS significantly and specifically reduces the in vivo response to adenosine challenge in a dose-dependent manner, is effective in protection against aeroallergen-induced bronchoconstriction (house dust mite), has an unexpected long-term duration of effect (8.3 days for both PC50 adenosine and resistance), and is free of side effects that might be toxic to the recipient. Such oligonucleotides may be used for treating a disease or condition associated with lung airway, such as bronchoconstriction, inflammation, or allergies.
AN 1999:219995 HCAPLUS <<LOGINID::20090206>>
DN 130:306599
TI Antisense oligonucleotides capable of binding to multiple targets and their use in the treatment of respiratory disease
IN Nyce, Jonathan W.
PA East Carolina University, USA
SO PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9913886	A1	19990325	WO 1998-US19419	19980917 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 20030087845	A1	20030508	US 1998-93972	19980609 <--
	US 6825174	B2	20041130		
	CA 2304312	A1	19990325	CA 1998-2304312	19980917 <--
	AU 9893951	A	19990405	AU 1998-93951	19980917 <--

	AU 752531	B2	20020919		
	EP 1019065	A1	20000719	EP 1998-947089	19980917 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	BR 9812650	A	20000822	BR 1998-12650	19980917 <--
	JP 2003517428	T	20030527	JP 2000-511506	19980917 <--
	MX 2000002640	A	20010930	MX 2000-2640	20000315 <--
	AU 2002050710	A	20020808	AU 2002-50710	20020628 <--
	US 20050014711	A1	20050120	US 2004-758451	20040114 <--
PRAI	US 1997-59160P	P	1997091?	<--	
	US 1998-93972	A	19980609	<--	
	US 1995-474497	A2	19950607	<--	
	US 1996-757024	A2	19961126	<--	
	WO 1998-US19419	W	19980917	<--	
	AU 2000-71749	A3	20001122	<--	

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 38 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Effects of intracellular cyclic AMP modulators on human eosinophil survival, degranulation and CD11b expression

AB Bronchial asthma is characterized by infiltration of inflammatory cells such as lymphocytes and eosinophils. Theophylline is one of the most widely used drugs in the therapy of bronchial asthma, and phosphodiesterase (PDE) inhibition is thought to be an important mechanism of its anti-inflammatory actions. However, the detailed effects of PDE inhibition on eosinophils still remain unclear. Eosinophils in peripheral blood obtained from normal subjects and patients with mild off-season allergic rhinitis were purified using CD16 neg. selection. The following effects of theophylline (nonselective PDE inhibitor), KF19514 (selective PDE IV inhibitor), mirlinone (selective PDE III inhibitor), procaterol (β2-adrenoceptor agonist) and N6, 2'-O-dibutyryladenosine 3',5'-cyclic monophosphate (dB-cAMP; AMP analog) on eosinophils were examined: (1) survival in the presence of interleukin-5, (2) degranulation by granulocyte/macrophage colony-stimulating factor (GM-CSF) or platelet-activating factor (PAF), (3) CD11b expression under GM-CSF or PAF stimulation and (4) intracellular cAMP level. Eosinophil survival was inhibited by theophylline, KF19514 or procaterol. GM-CSF- or PAF-induced degranulation was inhibited by theophylline, KF19514, procaterol or dB-cAMP. CD11b upregulation by PAF was inhibited by theophylline, KF19514 or dB-cAMP, while GM-CSF-stimulated CD11b up-regulation was not significantly inhibited by any of the drugs tested. The levels of intracellular cAMP were increased by theophylline, KF19514 and procaterol. Intracellular cAMP is an important factor in the regulation of eosinophil biol. functions. PDE IV inhibitors and β2-agonists are suggested to be useful for the treatment of bronchial asthma through inhibition of eosinophil effector function.

AN 1998:754166 HCAPLUS <<LOGINID::20090206>>

DN 130:177354

TI Effects of intracellular cyclic AMP modulators on human eosinophil survival, degranulation and CD11b expression

AU Momose, T.; Okubo, Y.; Horie, S.; Suzuki, J.; Isobe, M.; Sekiguchi, M.

CS First Department of Internal Medicine, Shinshu University School of Medicine, Matsumoto, 390-8621, Japan

SO International Archives of Allergy and Immunology (1998), 117(2), 138-145
CODEN: IAAIEG; ISSN: 1018-2438

PB S. Karger AG

DT Journal

LA English

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 39 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI The role of theophylline and phosphodiesterase 4 isoenzyme inhibitors as anti-inflammatory drugs
AB A review with 100 refs. Theophylline has been used for over a century in the treatment of asthma, and while it is used principally as a bronchodilator, a number of recent studies have demonstrated potential anti-inflammatory and immunomodulatory activity. Indeed, regular treatment with low-dose theophylline affords significant clin. benefit at the expense of unwanted side-effects associated with this drug, including headache and vomiting. The mechanism of action of theophylline is unclear, although a significant body of evidence points to an involvement of phosphodiesterase enzyme inhibition. Phosphodiesterases are a diverse group of enzymes that belong to ≥7 families, and of particular interest is the role of phosphodiesterase 4 isoenzyme, as it is distributed in a number of inflammatory and immune cells whose inhibition results in the down-regulation of inflammatory and immune cell function. The discovery of drugs selective for this isoenzyme has been viewed with interest in the light of pos. results from preclin. and early clin. studies. Whether orally active and safe phosphodiesterase 4 isoenzyme inhibitors will be useful in the treatment of asthma remains to be established.
AN 1998:588117 HCAPLUS <<LOGINID::20090206>>
DN 130:23
TI The role of theophylline and phosphodiesterase 4 isoenzyme inhibitors as anti-inflammatory drugs
AU Spina, D.; Landells, L. J.; Page, C. P.
CS The Sackler Institute of Pulmonary Pharmacology, The Department of Respiratory Medicine, Kings College School of Medicine and Dentistry, London, UK
SO Clinical and Experimental Allergy (1998), 28(8, Suppl. 3), 24-34
CODEN: CLEAEN; ISSN: 0954-7894
PB Blackwell Science Ltd.
DT Journal; General Review
LA English
RE.CNT 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 40 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Benzonaphthyridines as bronchial therapeutics
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = alkyl; R2, R3 = OH, alkoxy, cycloalkoxy, cycloalkylmethoxy, poly- or perfluoroalkoxy; or R2R3 = C1-2 alkylenedioxy; R4 = (un)substituted Ph] and salts are novel active bronchial therapeutics. The compds. are inhibitors of PDE3 and PDE4, and are particularly useful for treatment of airway disorders and dermatoses. Over 25 invention compds. were prepared and/or claimed. For example, the (-)-cis isomer of amide II (absolute configuration unknown) was cyclized by POCl3 in refluxing MeCN to give title compound III, isolated as the HCl salt in 70% yield. Selected I had -log IC50 (mol/L) values of 6.34-7.64 for PDE3 and 6.45-8.56 for PDE4, vs. much lower values for PDE1 (<4), PDE2 (4.80), and PDE5 (5.45).
AN 1998:341566 HCAPLUS <<LOGINID::20090206>>
DN 129:27934

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OREF 129:5955a,5958a
TI   Benzonaphthyridines as bronchial therapeutics
IN   Gutterer, Beate; Amschler, Hermann; Ulrich, Wolf-rudiger; Martin, Thomas;
     Bar, Thomas; Hatzelmann, Armin; Sanders, Karl; Beume, Rolf; Boss,
     Hildegard; Hafner, Dietrich; Kley, Hans-peter; Goebel, Karl-josef;
     Flockerzi, Dieter
PA   BYk Gulden Lomberg Chemische Fabrik G.m.b.H., Germany; Flockerzi, Dieter
SO   PCT Int. Appl., 37 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     -------------------  ----   --------    ---------------------  --------
PI   WO 9821208           A1     19980522    WO 1997-EP6096         19971105 <--
         W:  AL, AU, BA, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, JP, KR, LT,
             LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, VN, YU, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     CA 2270964            A1     19980522    CA 1997-2270964        19971105 <--
     CA 2270964            C      20070731
     AU 9853170            A      19980603    AU 1998-53170          19971105 <--
     AU 733129             B2     20010510
     EP 937074             A1     19990825    EP 1997-950093         19971105 <--
     EP 937074             B1     20030312
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             IE, SI, LT, LV, FI, RO
     CN 1236367            A      19991124    CN 1997-199529         19971105 <--
     CN 1090188            C      20020904
     BR 9713338            A      20000509    BR 1997-13338          19971105 <--
     NZ 334976             A      20001027    NZ 1997-334976         19971105 <--
     HU 2000000426         A2     20010228    HU 2000-426            19971105 <--
     HU 2000000426         A3     20010428
     JP 2001503442         T      20010313    JP 1998-522120         19971105 <--
     CZ 288752             B6     20010815    CZ 1999-1675           19971105 <--
     IL 129054             A      20020725    IL 1997-129054         19971105 <--
     EE 3829               B1     20020815    EE 1999-105            19971105 <--
     AT 234300             T      20030315    AT 1997-950093         19971105 <--
     SK 283269             B6     20030401    SK 1999-623            19971105 <--
     PT 937074             T      20030731    PT 1997-950093         19971105 <--
     ES 2195189            T3     20031201    ES 1997-950093         19971105 <--
     PL 189641             B1     20050930    PL 1997-333429         19971105 <--
     ZA 9710102            A      19980511    ZA 1997-10102          19971110 <--
     BG 103310             A      20000531    BG 1999-103310         19990405 <--
     BG 63695              B1     20020930
     US 6008215            A      19991228    US 1999-284458         19990416 <--
     KR 2000053100         A      20000825    KR 1999-704024         19990506 <--
     NO 9902282            A      19990511    NO 1999-2282           19990511 <--
     NO 312764             B1     20020701
     HK 1022151            A1     20030808    HK 2000-101112         20000224 <--
PRAI DE 1996-19646298      A      19961111  <--
     EP 1996-118188        A      19961113  <--
     DE 1997-19739056      A      19970905  <--
     WO 1997-EP6096        W      19971105  <--
OS   MARPAT 129:27934
RE.CNT  3     THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27  ANSWER 41 OF 48  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   The rabbit as an animal model of allergy, asthma and airway
     hyperresponsiveness
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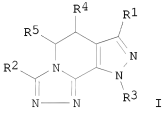
AB A review with 133 refs. discussing neonatal immunization, latex-induced hypersensitivity, allergic cutaneous responses, pulmonary function methodol., airway hyperresponsiveness, antigen-induced airway responses in vivo, inflammatory mediators, the effects of drugs on antigen-induced airway responses, airway hyperresponsiveness and airway wall remodeling, airway smooth muscle, IgE anaphylaxis, and sinusitis.
AN 1997:455304 HCAPLUS <<LOGINID::20090206>>
DN 127:134341
OREF 127:25893a,25896a
TI The rabbit as an animal model of allergy, asthma and airway hyperresponsiveness
AU Herd, C. M.; Page, C. P.
CS Biomedical Sciences Division, Pharmacology Group, King's College, University of London, London, SW3 6LX, UK
SO Allergy and Allergic Diseases (1997), Volume 2, 1079-1092. Editor(s): Kay, A. B. Publisher: Blackwell, Oxford, UK. CODEN: 64SCAU
DT Conference; General Review
LA English

L27 ANSWER 42 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Preparation of tricyclic 5,6-dihydro-9H-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-α]pyridines as inhibitors of phosphodiesterase (PDE) Type IV and the production of tumor necrosis factor (TNF)
GI



I

AB The title compds. [I; R1 = H, C1-6 alkyl, C1-6 alkoxy, etc.; R2, R3 = H, C1-14 alkyl, C2-14 alkenyl, etc.; R4, R5 = H, C1-6 alkyl, C1-6 alkoxy, etc.], useful in treating an inflammatory condition, asthma, arthritis, bronchitis, chronic obstructive airways disease, psoriasis, allergic rhinitis, dermatitis as well as AIDS, septic shock and other diseases, such as cachexia, were prepared Thus, reaction of 1-cyclopentyl-4,5-dihydro-3-ethyl-7-methylthio-1H-pyrazolo[3,4-c]pyridine with nicotinic acid hydrazide in pyridine afforded I [R1 = Et; R2 = 3-pyridyl; R3 = cyclopentyl; R4, R5 = H]. In general, compds. I are effective at 0.3-5 mg/kg/day.
AN 1997:94069 HCAPLUS <<LOGINID::20090206>>
DN 126:104095
OREF 126:20089a,20092a
TI Preparation of tricyclic 5,6-dihydro-9H-pyrazolo[3,4-c]-1,2,4-triazolo[4,3-α]pyridines as inhibitors of phosphodiesterase (PDE) Type IV and the production of tumor necrosis factor (TNF)
IN Duplantier, Allen J.; Cooper, Kelvin
PA Pfizer Inc., USA; Duplantier, Allen J.; Cooper, Kelvin
SO PCT Int. Appl., 31 pp. CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9639408	A1	19961212	WO 1995-IB429	19950606	<--
	W: CA, FI, JP, MX, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	CA 2223624	A1	19961212	CA 1995-2223624	19950606	<--
	CA 2223624	C	20010220			
	EP 837860	A1	19980429	EP 1995-918707	19950606	<--
	EP 837860	B1	20020320			
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	JP 10510242	T	19981006	JP 1996-511176	19950606	<--
	JP 3107827	B2	20001113			
	SK 282167	B6	20011106	SK 1996-718	19950606	<--
	AT 214700	T	20020415	AT 1995-918707	19950606	<--
	PT 837860	T	20020731	PT 1995-918707	19950606	<--
	ES 2172583	T3	20021001	ES 1995-918707	19950606	<--
	TW 460469	B	20011021	TW 1996-85105271	19960502	<--
	PL 184195	B1	20020930	PL 1996-314459	19960527	<--
	IL 118485	A	20000217	IL 1996-118485	19960530	<--
	IN 1996DE01159	A	20050311	IN 1996-DE1159	19960530	<--
	LV 11620	B	19970420	LV 1996-174	19960604	<--
	BR 9602627	A	19980901	BR 1996-2627	19960604	<--
	NO 9602320	A	19961209	NO 1996-2320	19960605	<--
	AU 9654773	A	19961219	AU 1996-54773	19960605	<--
	AU 694871	B2	19980730			
	HU 9601541	A2	19970228	HU 1996-1541	19960605	<--
	HU 9601541	A3	19970528			
	ZA 9604649	A	19971205	ZA 1996-4649	19960605	<--
	KR 191972	B1	19990615	KR 1996-20169	19960605	<--
	CZ 287251	B6	20001011	CZ 1996-1626	19960605	<--
	RU 2161158	C2	20001227	RU 1996-111027	19960605	<--
	CN 1142499	A	19970212	CN 1996-107630	19960606	<--
	CN 1061044	C	20010124			
	RO 115881	B1	20000728	RO 1996-1157	19960606	<--
	HR 960268	B1	20021231	HR 1996-268	19960606	<--
	AP 932	A	20010202	AP 1996-849	19960826	<--
	W: GM, BW, KE, MW, UG, ZM, ZW					
	FI 9704434	A	19971205	FI 1997-4434	19971205	<--
	FI 114097	B1	20040813			
	US 6004974	A	19991221	US 1998-973590	19980327	<--
	KR 225719	B1	19991015	KR 1998-44720	19981024	<--
PRAI	CA 1995-2223624	A	19950606	<--		
	EP 1995-918707	A	19950606	<--		
	WO 1995-IB429	A	19950606	<--		
	HU 1996-1541	A	19960605	<--		
	KR 1996-20169	A	19960605	<--		

OS MARPAT 126:104095
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 43 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Anti-inflammatory effects of theophylline and selective phosphodiesterase inhibitors
AB A review, with 101 refs. Theophylline has been used in the treatment of airway diseases, for more than 50 yr with benefit thought to be derived from its ability to elicit bronchodilatation. Recent evidence has, however, suggested that theophylline possesses anti-inflammatory activity. The mol. mechanism of action remains unclear, although

inhibition of the phosphodiesterase (PDE) enzyme, an enzyme which catalyzes the breakdown of cAMP and cGMP, has been proposed. Theophylline is a relatively weak inhibitor of PDE although there is evidence to suggest that PDE activity is elevated in leukocytes from patients with atopic disease. Thus, an altered responsiveness to PDE inhibitors may partly explain the mechanism of action of theophylline. The PDE enzyme exists as the least of seven different isoenzyme forms which can be characterized on the basis of a number of criteria including substrate specificity, sensitivity to selective inhibitors and the effect of allosteric modulators. The type IV isoenzyme is the predominant isoenzyme in inflammatory cells although it exists together with the type III isoenzyme in T-lymphocytes. There is considerable evidence from in vitro and in vivo studies suggesting that selective PDE IV inhibitors have anti-inflammatory activity. The following article reviews these studies, together with clin. studies demonstrating that theophylline has anti-inflammatory activity.

AN 1997:32991 HCAPLUS <<LOGINID::20090206>>
DN 126:69622
OREF 126:13321a,13324a
TI Anti-inflammatory effects of theophylline and selective phosphodiesterase inhibitors
AU Banner, Katharine H.; Page, Clive P.
CS Department Pharmacology, King's College London, London, SW3 6LX, UK
SO Allergology International (1996), 45(3), 125-132
CODEN: ALINFR; ISSN: 1323-8930
PB Blackwell
DT Journal; General Review
LA English
RE.CNT 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 44 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Phosphodiesterase inhibitors suppress proliferation of peripheral blood mononuclear cells and interleukin-4 and -5 secretion by human T-helper type 2 cells
AB It has been suggested that interleukin-4 and -5 (IL-4 and IL-5) are instrumental in the control of allergic disease. Elevated levels of IL-4 mRNA have been detected in numerous foci of atopic activity, including bronchoalveolar lavage (BAL) fluid from atopic asthmatics and skin of atopic dermatitis patients. IL-5 is important in eosinophil activation, which is a common feature of atopic disease. IL-5 mRNA has been detected in BAL fluid from both atopic and non-atopic asthmatics, indicating that IL-5 may be a common feature of the two disease states. Production of IL-4 and IL-5 by T cells appears to be associated with a high affinity cAMP phosphodiesterase (PDE). This study was designed to compare the effects of PDE inhibitors Ro20-1724 and theophylline on (1) the mitogenic response of peripheral blood mononuclear cells from atopic and non-atopic individuals and (2) secretion of IL-4 and IL-5 by TH2 cells after activation with PMA and anti-CD3. Both Ro20-1724 and theophylline inhibited proliferation of PBMC in a dose-dependent manner. There was no significant difference between proliferation of PBMC from atopic vs. non-atopic donors, but Ro20-1724, a specific PDE IV inhibitor, was more potent at a concentration of 10-5M than theophylline in suppressing lymphocyte proliferation. Similarly, both PDE inhibitors suppressed secretion of IL-4 and IL-5 from TH2-like cell lines in a dose-dependent manner. In conclusion, as Ro20-1724 and theophylline inhibit proliferation of PBMC and secretion of IL-4 and IL-5 from human TH2 cell lines, the development of a selective cyclic nucleotide PDE IV inhibitor may provide a promising new approach for asthma prophylaxis.
AN 1996:186716 HCAPLUS <<LOGINID::20090206>>

DN 124:278434
OREF 124:51211a,51214a
TI Phosphodiesterase inhibitors suppress proliferation of peripheral blood mononuclear cells and interleukin-4 and -5 secretion by human T-helper type 2 cells
AU Crocker, I. Caroline; Townley, Robert G.; Khan, Manzoor M.
CS Department of Medicine (Allergy Division), Creighton University Health Sciences Center, Omaha, Nebraska 68178, USA
SO Immunopharmacology (1996), 31(2-3), 223-35
CODEN: IMMUDP; ISSN: 0162-3109
PB Elsevier
DT Journal
LA English

L27 ANSWER 45 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Molecular mechanisms of antiasthma therapy
AB A review, with 35 refs. Recently there has been a much greater understanding of the mol. mechanisms involved in the actions of antiasthma therapy. β2-Agonists are the most effective bronchodilators and act predominantly on airway smooth muscle. Recent evidence suggests that β2-receptors in airway smooth muscle are coupled directly to maxi-K channels and may thereby bronchodilate without an increase in cAMP. The issue of β-receptor tolerance has been reawakened by the recognition that the protective effects of β2-agonists against bronchoconstrictor stimuli may become tolerant. Inhaled glucocorticoids are the mainstay of treatment in patients with chronic asthma. They suppress asthmatic inflammation predominantly by reducing transcription of genes coding for inflammatory mediators (particularly cytokines) and enzymes (inducible NO synthase, inducible cyclooxygenase). The inhibition of gene transcription is mediated predominantly by inhibition of transcription factors, such as activator protein-1 (AP-1) and nuclear factor-kappa B (NF-κB). There may be an abnormal activation of AP-1 in steroid-resistant asthma, and high concns. of β2-agonists may induce a secondary resistance by a interaction between the transcription factor CREB and the glucocorticoid receptor. Theophylline may have immunomodulatory effects that are more important than its bronchodilator action. Some effects of theophylline are mediated via inhibition of phosphodiesterases and several PDE IV inhibitors are currently undergoing evaluation in asthma.
AN 1996:88251 HCAPLUS <<LOGINID::20090206>>
DN 124:193043
OREF 124:35375a,35378a
TI Molecular mechanisms of antiasthma therapy
AU Barnes, Peter J.
CS Dep. Thoracic Medicine, National Heart Lung Inst., London, UK
SO Annals of Medicine (Helsinki) (1995), 27(5), 531-5
CODEN: ANMDEU; ISSN: 0785-3890
PB Blackwell
DT Journal; General Review
LA English

L27 ANSWER 46 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Theophylline and selective phosphodiesterase inhibitors as anti-inflammatory drugs in the treatment of bronchial asthma
AB A review with 50 refs. Theophylline has been in clin. use for the treatment of bronchial asthma and other respiratory diseases for well over 50 yrs. Over this time, a considerable body of evidence has accumulated to show that this drug has a wide range of pharmacol. actions, in addition to the well-recognized action on airway smooth muscle function. Current evidence suggests that part of the therapeutic value of theophylline in the treatment of asthma is by virtue of an anti-

inflammatory or immunomodulatory effect, although the actual mechanism of action remains unclear. The observed anti-inflammatory effects of theophylline could be attributed to phosphodiesterase (PDE) inhibition, and recently the type III and IV isoenzymes have been characterized in a number of inflammatory cells. This article reviews the evidence that theophylline and the newer more selective type IV PDE isoenzyme inhibitors can inhibit the activation of inflammatory cell types, such as T-lymphocytes, eosinophils, mast cells and macrophages, in vitro. The evidence supporting the ability of theophylline and selective PDE IV isoenzyme inhibitors to modify allergic inflammation both in animal models and clin. asthma is also discussed. Theophylline has important antiinflammatory and immunomodulatory activities and in light of this evidence, it is timely to reconsider the place of theophylline in the treatment of asthma.

AN 1995:756803 HCAPLUS <<LOGINID::20090206>>
DN 123:159861
OREF 123:28147a,28150a
TI Theophylline and selective phosphodiesterase inhibitors as anti-inflammatory drugs in the treatment of bronchial asthma
AU Banner, K.H.; Page, C.P.
CS Kings College, University of London, London, SW3 6LX, UK
SO European Respiratory Journal (1995), 8(6), 996-1000
CODEN: ERJOEI; ISSN: 0903-1936
PB Munksgaard
DT Journal; General Review
LA English

L27 ANSWER 47 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Effect of theophylline administered intratracheally as a dry powder formulation on bronchospasm and airway microvascular leakage in the anesthetized guinea pig
AB The effect of theophylline (a non-selective phosphodiesterase (PDE) inhibitor), dosed intratracheally (it) as a dry powder, on histamine- and platelet activating factor (Paf)-induced bronchospasm and antigen (ovalbumin, OA)-, histamine- and Paf-induced microvascular leakage (MVL) in the airways, was studied in the anesthetized guinea-pig. Bronchospasm was measured as the increase in pulmonary inflation pressure (PIP). MVL was assessed by fluorometric assay of fluorescein isothiocyanate dextran (FITC-dextran) content in airway tissues and tracheobronchial lavage fluid. OA (200 μg), histamine (60 nmol) and Paf (4 nmol), all given it, significantly increased MVL by up to 350% over levels in undosed unchallenged animals. Theophylline (50-500 μg it, n = 5-6) inhibited histamine-induced bronchospasm (30% ID, ID30: 258 ± 30 μg) and Paf-induced bronchospasm (ID30: 190 ± 80 μg). An inhibition of 40-50% of maximal bronchospasm was the largest attained. Theophylline, at approx. the bronchospasm ID30 dose (200 μg it, n = 4-8), inhibited MVL induced by all agents by 30-80% in airway tissues and in lavage fluid samples. Theophylline (50-500 μg it, n = 3) produced plasma drug levels of 0.13 ± 0.07 to 0.83 ± 0.39 μg/mL 10 min after dosing. Plasma levels were the same 60 min after dosing, suggesting retention of theophylline in the airways. The local concentration of theophylline retained in the airways should be sufficient to inhibit PDE activity. Direct application of theophylline (arguably by inhibition of the PDE isoforms PDE III, PDE IV and PDE V) thus has significant antiinflammatory and some bronchodilator effects at very low doses which should have no systemic toxicity. Theophylline applied as a dry powder locally in the airways may thus improve its documented usefulness in the treatment of asthma.

AN 1995:428226 HCAPLUS <<LOGINID::20090206>>

DN 122:178073
OREF 122:32389a,32392a
TI Effect of theophylline administered intratracheally as a dry powder formulation on bronchospasm and airway microvascular leakage in the anesthetized guinea pig
AU Raeburn, D.; Woodman, V. R.
CS Dagenham Res. Cent., Rhone-Poulenc Rorer Ltd., Dagenham/Essex, RM10 7XS, UK
SO Pulmonary Pharmacology (1994), 7(4), 243-9
CODEN: PUPHEX; ISSN: 0952-0600
PB Academic
DT Journal
LA English

L27 ANSWER 48 OF 48 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Phosphodiesterase inhibitors reduce bronchial hyperreactivity and airway inflammation in unrestrained guinea pigs
AB A new guinea pig model of allergic asthma was used to investigate the effects of low doses of the phosphodiesterase inhibitors, rolipram (phosphodiesterase IV selective), ORG 20241 (N-hydroxy-4-(3,4-dimethoxyphenyl)-thiazole-2-carboximidamide; dual phosphodiesterase III/IV inhibitor with some selectivity for the phosphodiesterase IV isoenzyme), and of theophylline (non-selective) on allergen-induced early and late phase asthmatic reactions, bronchial hyperreactivity to histamine inhalation, and airway inflammation. Theophylline (25 mg/kg i.p.) and ORG 20241 (5 mg/kg i.p.) did not affect histamine-induced bronchoconstriction, whereas rolipram (75 μg/kg i.p.) only slightly reduced the response to histamine at 7 h after administration. However, bronchial hyperreactivity after the early and after the late reaction was significantly reduced by theophylline, rolipram and ORG 20241, while bronchoalveolar lavage studies revealed a selective inhibition of airway inflammation by the phosphodiesterase inhibitors. Theophylline significantly reduced the number of eosinophils, neutrophils and macrophages; rolipram reduced the number of neutrophils and lymphocytes, and ORG 20241, the number of eosinophils and macrophages. None of the compds. at the dosage indicated reduced the early and late reaction when administered i.p. 1 h before allergen exposure to defined dual responding animals. These results indicate that non-bronchodilator doses of these phosphodiesterase inhibitors markedly reduce the allergen-induced development of bronchial hyperreactivity as well as airway inflammation, presumably by selectively inhibiting cellular migration. The results suggest that an orchestrated series of cellular interactions is involved in the development of bronchial hyperreactivity. It is concluded that phosphodiesterase inhibitors may be very useful in the treatment of bronchial asthma .
AN 1995:383469 HCAPLUS <<LOGINID::20090206>>
DN 122:178092
OREF 122:32393a,32396a
TI Phosphodiesterase inhibitors reduce bronchial hyperreactivity and airway inflammation in unrestrained guinea pigs
AU Santing, Ruud E.; Olymulder, Clemens G.; Van der Molen, Kees; Meurs, Herman; Zaagsma, Johan
CS Groningen/Utrecht Institute for Drug Exploration, Department of Medicinal Chemistry and Molecular Pharmacology, University of Groningen, A. Deusinglaan 2, AW Groningen, 9713, Neth.
SO European Journal of Pharmacology (1995), 275(1), 75-82
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier
DT Journal
LA English

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L8           0 S L7
L9           0 S L7 SSS FULL
L10            STRUCTURE UPLOADED
L11          0 S L10 FAM FULL
L12          1 S ROFLUMILAST/CN
L13          1 S THEOPHYLLINE/CN
L14          1 S TOFIMILAST/CN
L15          1 S PUMAFENTRINE/CN

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L20         31 S L16 AND L19
L21          9 S L20 AND (PY<2003 OR AY<2003 OR PRY<2003)
L22       3212 S PDE4 OR PDEIV OR (PDE 4) OR (PDE IV) OR (PHOSPHODIESTERASE(W)
L23        275 S L17 AND L22
L24         78 S L23 AND (PY<2002 OR AY<2002 OR PRY<2002)
L25          3 S L19 AND L24
L26     365584 S INFLAMM? OR ASTHMA OR COPD
L27         48 S L24 AND L26

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FULL ESTIMATED COST                                178.95     832.02

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                -43.46     -43.46

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PASSWORD:
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 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'HCAPLUS' AT 09:58:08 ON 06 FEB 2009
FILE 'HCAPLUS' ENTERED AT 09:58:08 ON 06 FEB 2009
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                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   178.95     832.02

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -43.46     -43.46

=> d l21 1-9 ti abs bib

L21  ANSWER 1 OF 9  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Aerosol inhalant formulations containing a diphenylpropionic acid scopine
     ester-type anticholinergic agent
GI
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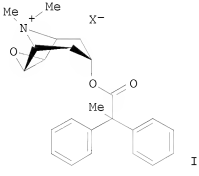

I

AB   The invention concerns a propellant-free aqueous aerosol inhalant containing a
     2,2-diphenylpropionic acid scopine ester anticholinergic agent
     of the formula (I), where X- represents an anion, especially chloride, bromide,
     4-toluene sulfonate, methanesulfonate. The formulations further contain
     an acid and benzalkonium chloride.


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AN   2004:220199  HCAPLUS <<LOGINID::20090206>>
DN   140:241079
TI   Aerosol inhalant formulations containing a diphenylpropionic acid scopine
     ester-type anticholinergic agent
IN   Schmidt, Friedrich
PA   Boehringer Ingelheim Pharma GmbH & Co. Kg, Germany
SO   PCT Int. Appl., 23 pp.
     CODEN: PIXXD2
DT   Patent
LA   German
FAN.CNT 2
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PI   WO 2004022052        A1    20040318    WO 2003-EP8221         20030725 <--
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             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
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             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
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     AU 2003298473        A1    20040329    AU 2003-298473         20030725 <--
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     EP 1530464           B1    20080709
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PRAI DE 2002-10237232     A     20020814  <--
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     WO 2003-EP8221       W     20030725
OS   MARPAT 140:241079
RE.CNT  3     THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21  ANSWER 2 OF 9  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Inhalants containing 2,2-diphenylpropionic acid scopine ester N-metho
     salts as anticholinergic agent in combination with
     corticosteroids and betamimetics
AB   The invention concerns inhalants that contain 2,2-diphenylpropionic acid
     scopine ester N-metho salts, especially 2,2-diphenylpropionic acid scopine
ester
     methobromide in combination with corticosteroids and betamimetics for the
     treatment of asthma and COPD.  Thus an inhalation powder contained
     (μg/capsule): 2,2-diphenylpropionic acid scopine ester methobromide
     100; budesonide 200; salmeterolxinafoate 55.0; lactose 4721.6.
AN   2004:158987  HCAPLUS <<LOGINID::20090206>>
DN   140:205135
TI   Inhalants containing 2,2-diphenylpropionic acid scopine ester N-metho
     salts as anticholinergic agent in combination with
     corticosteroids and betamimetics
IN   Meade, Christopher John Montague; Pairet, Michel; Pieper, Michael P.
PA   Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SO   Ger. Offen., 22 pp.
     CODEN: GWXXBX
DT   Patent
LA   German
FAN.CNT 1
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PI   DE 10237739         A1     20040226    DE 2002-10237739       20020817 <--
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     US 7244742          B2     20070717
     CA 2495454          A1     20040318    CA 2003-2495454        20030725 <--
     WO 2004022058       A1     20040318    WO 2003-EP8222         20030725 <--
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
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             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
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     EP 1530471           B1    20070711
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     CN 1688308           A     20051026    CN 2003-823798         20030725 <--
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     EP 1785136           A2    20070516    EP 2007-103257         20030725 <--
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     AT 366574            T     20070815    AT 2003-793643         20030725 <--
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     IN 2005DN00510       A     20090116    IN 2005-DN510          20050210 <--
     MX 2005001823        A     20050419    MX 2005-1823           20050215 <--
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PRAI DE 2002-10237739     A     20020817  <--
     US 2002-413177P      P     20020924  <--
     US 2003-625129       A3    20030723
     EP 2003-793643       A3    20030725
     WO 2003-EP8222       W     20030725
OS   MARPAT 140:205135

L21  ANSWER 3 OF 9  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Aerosol inhalant formulations containing a diphenylpropionic acid scopine
     ester-type anticholinergic agent
GI
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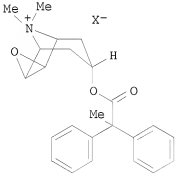

I

AB   The invention concerns a propellant-free aqueous aerosol inhalant containing a 2,2-diphenylpropionic acid scopine ester anticholinergic agent of the formula (I), where X- represents an anion, especially chloride, bromide, 4-toluene sulfonate, methanesulfonate. The formulations further contain an acid and benzalkonium chloride.

AN   2004:158961 HCAPLUS <<LOGINID::20090206>>

DN 140:205134
TI Aerosol inhalant formulations containing a diphenylpropionic acid scopine ester-type anticholinergic agent
IN Schmidt, Friedrich
PA Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SO Ger. Offen., 8 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

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	JP 2006506345	T	20060223	JP 2004-533274	20030725	<--
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	AT 400265	T	20080715	AT 2003-740479	20030725	<--
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	US 20040166065	A1	20040826	US 2003-637769	20030808	<--
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PRAI	DE 2002-10237232	A	20020814	<--		
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	WO 2003-EP8221	W	20030725			
	US 2003-637769	A1	20030808			

OS MARPAT 140:205134

L21 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Pharmaceutical compositions for the treatment of respiratory tract diseases comprising novel anticholinergic agents and inhibitors of EGFR-kinase
AB The invention relates to novel pharmaceutical compns. comprising novel anticholinergic agents and EGFR-kinase inhibitors, method for production and use thereof in the treatment of respiratory diseases. The synthesis of several EGFR-kinase inhibitors is given. Thus an inhalation capsule contained (microgram/capsule): 2,2-Diphenylpropionic acid scopine

ester methobromide 60; EGFR kinase inhibitor 3500; lactose 3440.

AN 2004:41317 HCAPLUS <<LOGINID::20090206>>

DN 140:99649

TI Pharmaceutical compositions for the treatment of respiratory tract diseases comprising novel anticholinergic agents and inhibitors of EGFR-kinase

IN Pairet, Michel; Meade, Christopher John Montague; Pieper, Michael P.

PA Boehringer Ingelheim Pharma Gmbh & Co. Kg, Germany

SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

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PI	WO 2004004775	A1	20040115	WO 2003-EP6788	20030626 <--
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	EP 2003-762525	A3	20030626		
	WO 2003-EP6788	W	20030626		
	US 2003-614382	A1	20030707		

OS MARPAT 140:99649

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Pharmaceutical compositions based on novel anticholinergics and p38 kinase inhibitors

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to novel pharmaceutical compns. based on novel anticholinergics and p38 kinase inhibitors, processes for preparing them and their use in the treatment of respiratory diseases. Inhalation powders were prepared containing anticholinergic I and p38 kinase inhibitor II.
AN 2004:41274 HCAPLUS <<LOGINID::20090206>>
DN 140:99644
TI Pharmaceutical compositions based on novel anticholinergics and p38 kinase inhibitors
IN Pairet, Michel; Meade, Christopher John Montague; Pieper, Michael P.
PA Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SO PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
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	ES 2278170	T3	20070801	ES 2003-738089	20030626	<--
	US 20040044020	A1	20040304	US 2003-611717	20030701	<--
	US 20050163726	A1	20050728	US 2005-68204	20050228	<--
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	WO 2003-EP6739	W	20030626			
	US 2003-611717	A1	20030701			

OS MARPAT 140:99644
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Pharmaceutical compositions comprising novel anticholinergic agents and NK1-receptor antagonists for the treatment of respiratory tract diseases

AB The invention relates to novel pharmaceutical compns. comprising novel anticholinergic agents and NK1-receptor antagonists, method for production and use thereof in the treatment of respiratory diseases. Thus an inhalation capsule contained (microgram/capsule): 2,2-Diphenylpropionic acid scopine ester methobromide 200; N-[2-(3,5-Bis-trifluoromethylphenyl)-ethyl]-2-{4-[(3-hydroxypropyl)methylamino]piperidin-1-yl}-N-methyl-2-phenylacetamide 150; lactose 12150.

AN 2004:41273 HCAPLUS <<LOGINID::20090206>>

DN 140:99643

TI Pharmaceutical compositions comprising novel anticholinergic agents and NK1-receptor antagonists for the treatment of respiratory tract diseases

IN Pairet, Michel; Meade, Christopher John Montague; Pieper, Michael P.

PA Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany

SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
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	US 20040048886	A1	20040311	US 2003-614362	20030707	<--
PRAI	DE 2002-10230750	A	20020709	<--		
	US 2002-407758P	P	20020903	<--		
	WO 2003-EP6667	W	20030625			

OS MARPAT 140:99643

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Pharmaceutical compositions comprising anticholinergic agents and phosphodiesterase IV (PDE-IV) inhibitors for the treatment of respiratory diseases

AB The invention provides pharmaceutical compns. comprising anticholinergic agents and PDE-IV inhibitors, as well as a method for the production and use thereof in the treatment of respiratory diseases. Powder inhalant formulations are included.

AN 2004:41257 HCAPLUS <<LOGINID::20090206>>

DN 140:87709

TI Pharmaceutical compositions comprising anticholinergic agents and phosphodiesterase IV (PDE-IV) inhibitors for the treatment of respiratory diseases
IN Pairet, Michel; Meade, Christopher John Montague; Pieper, Michael P.
PA Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2004004704	A1	20040115	WO 2003-EP6668	20030625	<--
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
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	CA 2492026	A1	20040115	CA 2003-2492026	20030625	<--
	AU 2003242755	A1	20040123	AU 2003-242755	20030625	<--
	EP 1521576	A1	20050413	EP 2003-762509	20030625	<--
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	US 20040058950	A1	20040325	US 2003-614365	20030707	<--
PRAI	DE 2002-10230769	A	20020709	<--		
	US 2002-407895P	P	20020903	<--		
	WO 2003-EP6668	W	20030625			

OS MARPAT 140:87709
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Pharmaceutical combinations containing heterocyclic compounds and scopine diphenyl propionate as anticholinergic agent
AB The invention concerns pharmaceutical combinations that contain heterocyclic compds., especially benzofuran and benzopyran derivs., and scopine di-Ph propionate or its salts as an anticholinergic agent; the compns. are formulated as inhalants and are used for the treatment of respiratory tract diseases. Thus a microcapsule included (μg): scopine diphenylpropionate methobromide 200; heterocyclic compound 200; lactose 4600.
AN 2003:837039 HCAPLUS <<LOGINID::20090206>>
DN 139:328380
TI Pharmaceutical combinations containing heterocyclic compounds and scopine diphenyl propionate as anticholinergic agent
IN Banholzer, Rolf; Meade, Christopher John Montague; Meissner, Helmut; Morschhaeuser, Gerd; Pairet, Michel; Pieper, Michael P.; Pohl, Gerald; Reichl, Richard; Speck, Georg
PA Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003087049	A2	20031023	WO 2003-EP3670	20030409 <--
	WO 2003087049	A3	20040205		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE 10216427	A1	20031023	DE 2002-10216427	20020412 <--
	US 20040002502	A1	20040101	US 2003-409402	20030408 <--
	AU 2003221562	A1	20031027	AU 2003-221562	20030409 <--
PRAI	DE 2002-10216427	A	20020412	<--	
	WO 2003-EP3670	W	20030409		

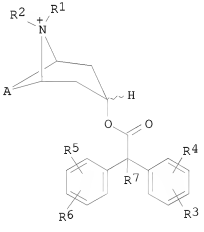
OS MARPAT 139:328380

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Procedures for the production of new anticholinergic alkaloids as well as for their use in medicines

GI



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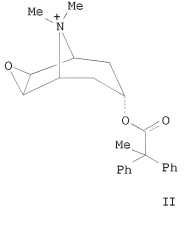

II

AB The present invention concerns new anticholinergics I·X- [A = CH2CH2, CH:CH, oxirane-2,3-diyl; X- = simple anion; R1, R2 = C1-4-alkyl, C1-4-hydroxyalkyl, C1-4-haloalkyl; R3 - R6 = H, C1-4-alkyl, C1-4-alkoxy, OH, CF3, CN, NO2, halogen; R7 = H, C1-4-alkyl, C1-4-alkyloxy, C1-4-haloalkylene, C1-4-haloalkoxy, C1-4-hydroxyalkylene, CF3, C1-4-alkylene- C1-4-alkoxy, OC(:O)-, C1-4-alkyl, OC(:O)-, C1-4-haloalkyl, OC(:O)CF3, halogen] and their physiol. acceptable salts, procedures for their production as well as their use as drugs. Thus, scopine ester II·Br- was prepared from Ph2CMeCO2H via acyl chloride formation with (COCl)2 in CH2Cl2 containing catalytic Me2NCHO, esterification with scopine in CH2Cl2, and quaternization with MeBr in MeCN/CH2Cl2. Pharmaceutical

formulations for use as tablets, in ampuls, in aerosols, in solution and as inhalants are presented.

AN 2002:291677 HCAPLUS <<LOGINID::20090206>>

DN 136:325718

TI Procedures for the production of new anticholinergic alkaloids as well as for their use in medicines

IN Meissner, Helmut; Morschhaeuser, Gerd; Pieper, Helmut; Pohl, Gerald; Reichl, Richard; Speck, Georg; Banholzer, Rolf

PA Boehringer Ingelheim Pharma K.-G., Germany

SO Ger. Offen., 16 pp.
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	DE 10050994	A1	20020418	DE 2000-10050994	20001014	<--
	WO 2002032899	A1	20020425	WO 2001-EP11226	20010928	<--
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	EE 200300151	A	20030616	EE 2003-151	20010928	<--
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	EP 1325001	B1	20040218			
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	HU 2003001203	A3	20060529			
	EP 1382606	A2	20040121	EP 2003-23933	20010928	<--
	EP 1382606	A3	20041013			
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	AT 259805	T	20040315	AT 2001-982374	20010928	<--
	JP 2004511557	T	20040415	JP 2002-536281	20010928	<--
	JP 4109106	B2	20080702			
	PT 1325001	T	20040730	PT 2001-982374	20010928	<--
	NZ 525836	A	20040924	NZ 2001-525836	20010928	<--
	ES 2215147	T3	20041001	ES 2001-982374	20010928	<--
	CN 1275962	C	20060920	CN 2001-817144	20010928	<--
	AU 2002213975	B2	20061109	AU 2002-213975	20010928	<--
	US 20020115680	A1	20020822	US 2001-976950	20011011	<--
	US 6706726	B2	20040316			
	BG 107688	A	20030930	BG 2003-107688	20030328	<--
	IN 2003DN00538	A	20070427	IN 2003-DN538	20030409	<--
	MX 2003003160	A	20050909	MX 2003-3160	20030410	<--
	NO 2003001693	A	20030528	NO 2003-1693	20030411	<--
	ZA 2003002914	A	20031114	ZA 2003-2914	20030411	<--
	HR 2003000278	B1	20060228	HR 2003-278	20030411	<--
	KR 830359	B1	20080520	KR 2003-705256	20030414	<--
	US 20040087617	A1	20040506	US 2003-684994	20031014	<--
	HK 1060566	A1	20061229	HK 2004-103582	20040520	<--

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     US 20050197357       A1    20050908    US 2005-117163          20050428 <--
     JP 2008120834        A     20080529    JP 2008-33492           20080214 <--
PRAI DE 2000-10050994     A     20001014  <--
     US 2000-252777P      P     20001122  <--
     EP 2001-982374       A3    20010928  <--
     JP 2002-536281       A3    20010928  <--
     WO 2001-EP11226      W     20010928  <--
     US 2001-976950       A1    20011011  <--
     US 2003-684994       A1    20031014
OS   CASREACT 136:325718; MARPAT 136:325718
RE.CNT  1     THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d his

     (FILE 'HOME' ENTERED AT 09:10:50 ON 06 FEB 2009)

     FILE 'REGISTRY' ENTERED AT 09:10:56 ON 06 FEB 2009
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L3            33 S L1 SSS FULL
L4               STRUCTURE UPLOADED
L5             2 S L4
L6            91 S L4 SSS FULL
L7               STRUCTURE UPLOADED
L8             0 S L7
L9             0 S L7 SSS FULL
L10              STRUCTURE UPLOADED
L11            0 S L10 FAM FULL
L12            1 S ROFLUMILAST/CN
L13            1 S THEOPHYLLINE/CN
L14            1 S TOFIMILAST/CN
L15            1 S PUMAFENTRINE/CN

     FILE 'HCAPLUS' ENTERED AT 09:14:09 ON 06 FEB 2009
L16           38 S L3 SSS FULL
L17         3374 S L6/THU OR L13/THU OR L14/THU OR L12/THU OR L15/THU
L18            2 S L16 AND L17
L19         5523 S ANTICHOLINERGIC
L20           31 S L16 AND L19
L21            9 S L20 AND (PY<2003 OR AY<2003 OR PRY<2003)
L22         3212 S PDE4 OR PDEIV OR (PDE 4) OR (PDE IV) OR (PHOSPHODIESTERASE(W)
L23          275 S L17 AND L22
L24           78 S L23 AND (PY<2002 OR AY<2002 OR PRY<2002)
L25            3 S L19 AND L24
L26       365584 S INFLAMM? OR ASTHMA OR COPD
L27           48 S L24 AND L26

=> log hold
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                  ENTRY    SESSION
FULL ESTIMATED COST                               208.80     861.87

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CA SUBSCRIBER PRICE                               -50.84     -50.84

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SESSION RESUMED IN FILE 'HCAPLUS' AT 10:28:55 ON 06 FEB 2009
FILE 'HCAPLUS' ENTERED AT 10:28:55 ON 06 FEB 2009
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FULL ESTIMATED COST	208.80	861.87

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-50.84	-50.84

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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DICTIONARY FILE UPDATES: 4 FEB 2009 HIGHEST RN 1100909-82-7

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http://www.cas.org/support/stngen/stndoc/properties.html

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.48	862.35

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)       SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                  0.00     -50.84

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FILE COVERS 1907 - 6 Feb 2009  VOL 150 ISS 7
FILE LAST UPDATED: 5 Feb 2009  (20090205/ED)

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

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http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.

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             6 L6
       1091697 THU/RL
L28          6 L6/THU
                 (L6 (L) THU/RL)

=> s l22 and l28
L29          3 L22 AND L28

=> d l28 1-6 ti abs bib

L28  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2009 ACS on STN
TI   Treatment for depression and anxiety by the combination of a PDE IV
     inhibitor and an antidepressant or an anxiolytic agent
AB   The present invention relates to a method of treating depression or
     anxiety in a mammal, including a human, by administering to the mammal a
     PDE IV inhibitor in combination with an antidepressant or an anxiolytic
     agent.  It also relates to pharmaceutical compns. containing a
     pharmaceutically acceptable carrier, a PDE IV inhibitor and an anxiolytic
     agent or antidepressant.
AN   2003:1006815  HCAPLUS <<LOGINID::20090206>>
DN   140:35974
TI   Treatment for depression and anxiety by the combination of a PDE IV
     inhibitor and an antidepressant or an anxiolytic agent
IN   Sobolov-Jaynes, Susan Beth; Schmidt, Christopher Joseph
PA   Pfizer Products Inc., USA
SO   PCT Int. Appl., 62 pp.
```

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003105902	A1	20031224	WO 2003-IB2295	20030605
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
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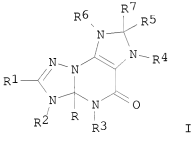
US 20030235631	A1	20031225	US 2003-387060	20030312
CA 2488138	A1	20031224	CA 2003-2488138	20030605
AU 2003233032	A1	20031231	AU 2003-233032	20030605
EP 1517707	A1	20050330	EP 2003-727833	20030605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003011903	A	20050607	BR 2003-11903	20030605
JP 2005533788	T	20051110	JP 2004-512802	20030605
MX 2004011835	A	20050331	MX 2004-11835	20041126
IN 2004CN03177	A	20060303	IN 2004-CN3177	20041213
PRAI US 2002-389181P	P	20020617		
WO 2003-IB2295	W	20030605		

OS MARPAT 140:35974
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Preparation of imidazotriazolopyrimidines as adenosine receptor antagonists
GI



I

AB Title compds. [I; R1 = H, alkyl, phenyl(alkyl), alkoxycarbonyl, etc.; R2 or R3 = alkyl, alkenyl, benzyl; RR2 or RR3 = bond; R4 or R6 = H, alkyl(amino), CH2Ph, etc.; R4R7 or R6R7 = bond; R5 = H, alkyl, phenyl(alkyl), etc.] were prepared Thus,7-amino-2-[(4-methoxybenzyloxy)methyl]-s-triazolo[1,5-a]pyrimidine-5-one was converted in 10 steps to I (RR2 = bond, R1 = CH2OPh, R3 = Et, R4 or R6 = H, R4R7 or R6R7 = bond, R5 = cyclopentyl). Data for biol. activity of I were given.
AN 2002:942787 HCAPLUS <<LOGINID::20090206>>

DN 138:14073
TI Preparation of imidazotriazolopyrimidines as adenosine receptor antagonists
IN Blech, Stefan; Carter, Adrian; Gaida, Wolfram; Hoffmann, Matthias; Kuefner-Muehl, Ulrike; Meade, Christopher John Montague; Pohl, Gerald; Kummer, Werner; Lehr, Erich; Mierau, Joachim; Weiser, Thomas
PA Boehringer Ingelheim Pharma KG, Germany
SO U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 333,621, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6492377	B1	20021210	US 2000-559806	20000426
	WO 2000012511	A1	20000309	WO 1998-EP5455	19980827
	W: AU, BG, BR, BY, CA, CN, CZ, EE, HU, ID, IL, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN, AM, AZ, KG, MD, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	ZA 9808189	A	20000110	ZA 1998-8189	19980908
	BR 9900187	A	20000502	BR 1999-187	19990127
	MX 9905843	A	20000331	MX 1999-5843	19990621
PRAI	US 1998-90586P	P	19980625		
	US 1998-90587P	P	19980625		
	WO 1998-EP5455	A2	19980827		
	US 1999-333408	A2	19990615		
	US 1999-333621	B2	19990615		

OS MARPAT 138:14073
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Inhalant compositions containing anticholinergics and PDE IV inhibitors
AB The invention relates to drug compns. based on anticholinergics and PDE IV inhibitors, to methods for their production, and to their use as inhalants for the treatment of respiratory tract diseases. Thus an inhalation powder was composed of capsules that contained (μg/capsule): tiotropium bromide 21.7; AWD-12-281 200; lactose 4778.3.
AN 2002:695761 HCAPLUS <<LOGINID::20090206>>
DN 137:237718
TI Inhalant compositions containing anticholinergics and PDE IV inhibitors
IN Meade, Christopher John Montague; Pairet, Michel; Pieper, Michael Paul
PA Boehringer Ingelheim Pharma K.-G., Germany
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 19

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002069945	A2	20020912	WO 2002-EP1988	20020226
	WO 2002069945	A3	20030130		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,				

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	DE 10110772	A1	20020912	DE 2001-10110772	20010307
	CA 2439763	A1	20020912	CA 2002-2439763	20020226
	AU 2002257587	A1	20020919	AU 2002-257587	20020226
	AU 2002257587	B2	20070510		
	EP 1372649	A2	20040102	EP 2002-727329	20020226
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004521134	T	20040715	JP 2002-569122	20020226
	BR 2002007883	A	20040727	BR 2002-7883	20020226
	HU 2004000782	A2	20040728	HU 2004-782	20020226
	NZ 528621	A	20050429	NZ 2002-528621	20020226
	CN 1649588	A	20050803	CN 2002-805346	20020226
	ZA 2003006221	A	20040722	ZA 2003-6221	20030812
	IN 2003DN01295	A	20050527	IN 2003-DN1295	20030814
	MX 2003008045	A	20031204	MX 2003-8045	20030905
	AU 2008202554	A1	20080703	AU 2008-202554	20080610
PRAI	DE 2001-10110772	A	20010307		
	WO 2002-EP1988	W	20020226		
	AU 2006-202723	A3	20060626		

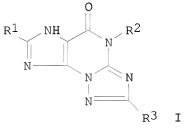
OS MARPAT 137:237718

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN

TI Tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors

GI



I

AB Tricyclic N heterocycles I [R1 = C1-5 alkyl, C5-6 cycloalkyl, Ph, PhCH2, 5- or 6-membered heterocyclic ring; R2 = C1-5 alkyl, C2-4 alkenyl; R3 = (substituted) C1-5 alkyl, (substituted) C5-6 cycloalkyl] and their salts are phosphodiesterase IV inhibitors and are potentially useful as vasodilators, inflammation inhibitors, and antiallergic agents. Thus, I (R1 = cyclopentyl, R2 = n-Pr, R3 = i-Pr) inhibited human monocyte phosphodiesterase IV with an IC50 of 0.018 μm. A tablet formulation contained I 80, corn starch 190, lactose 55, microcryst. cellulose 35, PVP 15, Na carboxymethylstarch 23, and Mg stearate 2 mg.

AN 2000:420941 HCAPLUS <<LOGINID::20090206>>

DN 133:53696

TI Tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors

IN Hoffmann, Matthias; Jung, Birgit; Kuefner-Muehl, Ulrike; Meade, Christopher John Montague

PA Boehringer Ingelheim Pharma K.-G., Germany

SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2

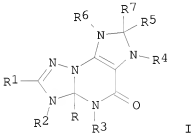
DT Patent

LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000035428	A2	20000622	WO 1999-EP9086	19991124
	WO 2000035428	A3	20000928		
	W: CA, JP, MX, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	DE 19858331	A1	20000621	DE 1998-19858331	19981217
	CA 2345752	A1	20000622	CA 1999-2345752	19991124
	EP 1140098	A2	20011010	EP 1999-959324	19991124
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6417190	B1	20020709	US 1999-458789	19991210
	MX 2001005936	A	20011203	MX 2001-5936	20010612
PRAI	DE 1998-19858331	A	19981217		
	US 1999-127777P	P	19990405		
	WO 1999-EP9086	W	19991124		

OS MARPAT 133:53696
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Preparation of imidazotriazolopyrimidines as adenosine receptor antagonists
GI



I

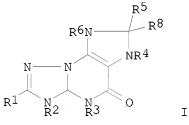
AB Title compds. [I; R1 = H, alkyl, phenyl(alkyl), alkoxycarbonyl, etc.; R2 or R3 = H, alkyl, phenylalkyl, heterocyclyl(alkyl), etc.; RR2 or RR3 = bond; R4 or R6 = H, (amino)alkyl, CH2Ph, etc.; R4R7 or R6R7 = bond; R5 = H, alkyl, phenyl(alkyl), etc.] were prepared Thus,7-amino-2-[(4-methoxybenzyloxy)methyl]-s-triazolo[1,5-a]pyrimidine-5-one was converted in 10 steps to I (RR2 = bond, R1 = CH2OPh, R3 = Et, R4 or R6 = H, R4R7 or R6R7 = bond, R5 = cyclopentyl). Data for biol. activity of I were given.
AN 2000:161287 HCAPLUS <<LOGINID::20090206>>
DN 132:194388
TI Preparation of imidazotriazolopyrimidines as adenosine receptor antagonists
IN Kufner-muhl, Ulrike; Kummer, Werner; Pohl, Gerald; Gaida, Wolfram; Lehr, Erich; Mierau, Joachim; Weiser, Thomas; Carter, Adrian; Meade, Christopher John Montague; Blech, Stefan; Hoffmann, Matthias
PA Boehringer Ingelheim Pharma Kg, Germany; et al.

SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000012511	A1	20000309	WO 1998-EP5455	19980827
W: AU, BG, BR, BY, CA, CN, CZ, EE, HU, ID, IL, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN, AM, AZ, KG, MD, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9893474	A	20000321	AU 1998-93474	19980827
US 6492377	B1	20021210	US 2000-559806	20000426
PRAI US 1998-90586P	P	19980625		
US 1998-90587P	P	19980625		
WO 1998-EP5455	A	19980827		
US 1999-333408	A2	19990615		
US 1999-333621	B2	19990615		

OS MARPAT 132:194388
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
TI Imidazotriazolopyrimidines as adenosine antagonists
GI



I

AB Imidazotriazolopyrimidines I [R1, R5 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, Ph, norbornyl, norbornenyl, adamantyl, noradamantyl, CO2H, CONH2, NH2, CHO; R2, R3 = (un)substituted alkyl; R2R7, R3R7, R4R8, R8R6 = bond; R4, R6 = H, alkyl, aminoalkyl, PhCH2; R2 and R3 or R4 and R6 cannot be present simultaneously] were prepared for use as adenosine antagonists. Thus, I [R1 = CH2OPh, R2R7, R4R8 = bond, R3 = Et, R5 = cyclopentyl, R4R8 = bond, II] was prepared from 4-MeOC6H4CH2OH, ClCH2CO2H, aminoguanidine cyclopentanecarbonyl chloride, and phenol in 12 steps. II had a KiA1 receptor binding activity of 3.6 nM.
AN 1999:811248 HCAPLUS <<LOGINID::20090206>>
DN 132:35717
TI Imidazotriazolopyrimidines as adenosine antagonists
IN Blech, Stefan; Carter, Adrian; Gaida, Wolfram; Hoffmann, Matthias; KuefnerMuehl, Ulrike; Meade, Christopher John Montague; Pohl, Gerald
PA Boehringer Ingelheim Pharma K.-G., Germany
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent

LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9965912	A1	19991223	WO 1999-EP4017	19990611
	W: AU, BG, BR, BY, CA, CN, CZ, EE, HU, ID, IL, IN, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN, YU, ZA, AM, AZ, KG, MD, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	DE 19826843	A1	19991223	DE 1998-19826843	19980616
	CA 2327395	A1	19991223	CA 1999-2327395	19990611
	CA 2327395	C	20080513		
	AU 9945112	A	20000105	AU 1999-45112	19990611
	EP 1087973	A1	20010404	EP 1999-927950	19990611
	EP 1087973	B1	20030108		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002518396	T	20020625	JP 2000-554737	19990611
	AT 230748	T	20030115	AT 1999-927950	19990611
	ES 2186369	T3	20030501	ES 1999-927950	19990611
	MX 2000010236	A	20010507	MX 2000-10236	20001019
PRAI	DE 1998-19826843	A	19980616		
	WO 1999-EP4017	W	19990611		

OS MARPAT 132:35717
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT